Atrial Fibrillation Overview and Updates

Jim Liu, MD, FACC
Assistant Professor - Clinical
Department of Internal Medicine
Division of Cardiovascular Medicine
The Ohio State University Wexner Medical Center

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Center for Continuing Medical Education

The Ohio State University
Wexner Medical Center

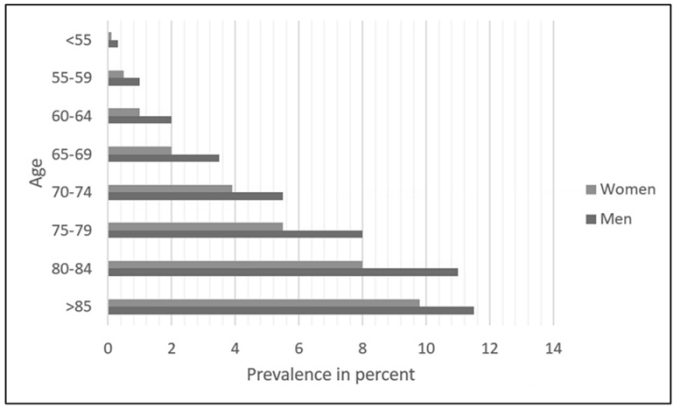
Objectives

1. Review Afib evaluation
2. Recognize importance of lifestyle and risk factor modification
3. Discuss stroke prevention
4. Understand differences in rate and rhythm management

Why is Afib important?

- 3-6 million people estimated to have Afib in the US
- Projected to increase to 6-16 million by 2050
- Lifetime risk of developing Afib from age 40-95:
  - 26% for men
  - 23% for women

Prevalence of Afib by age



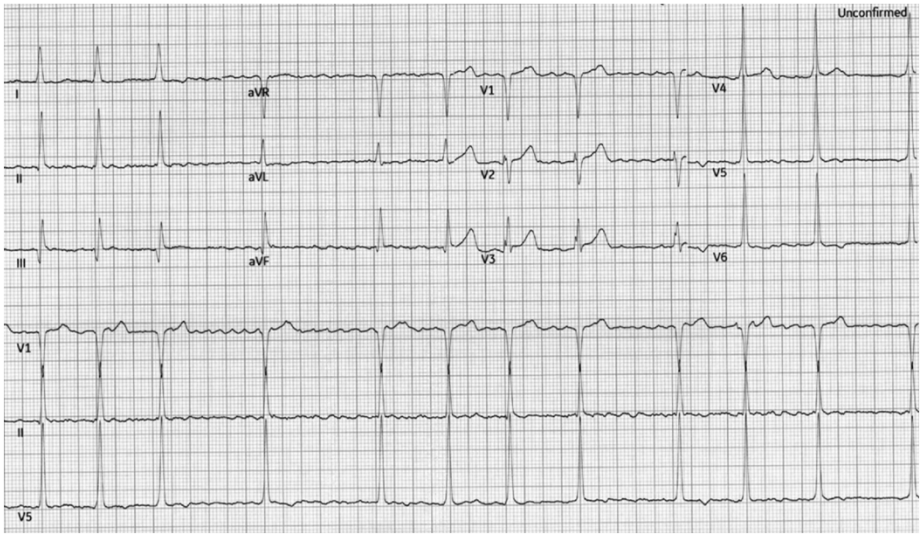
Why is Afib important?

- >467,000 annual hospitalizations
- 2x as likely to be hospitalized
- >99,000 deaths per year

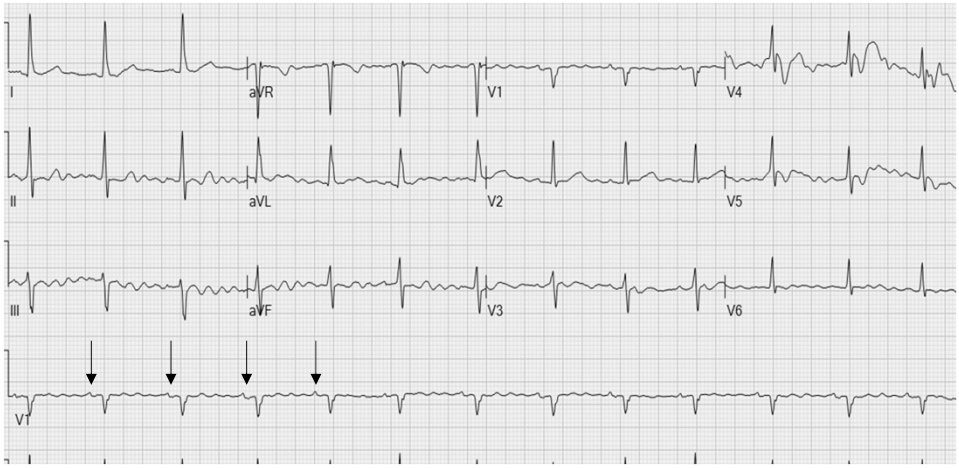
- Adds $8,700 per year per patient
- Adds $26 billion to US healthcare annually

What is Afib?

1. Irregularly irregular R-R intervals
2. Absence of distinct repeating P waves
3. Irregular atrial activity

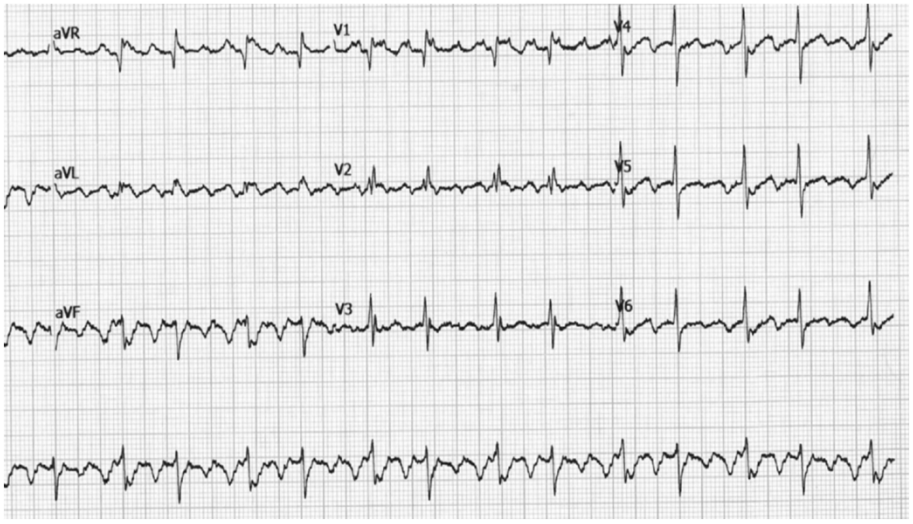


What is not Afib?



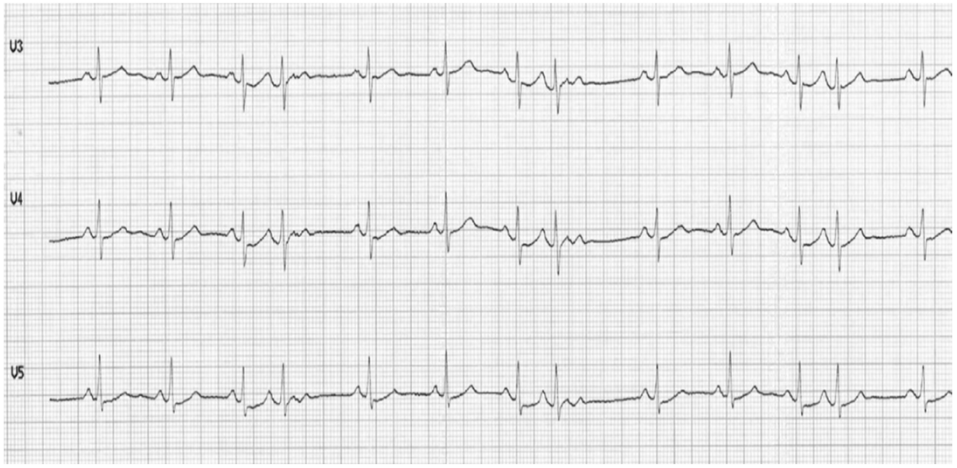
Artifact

What is not Afib?



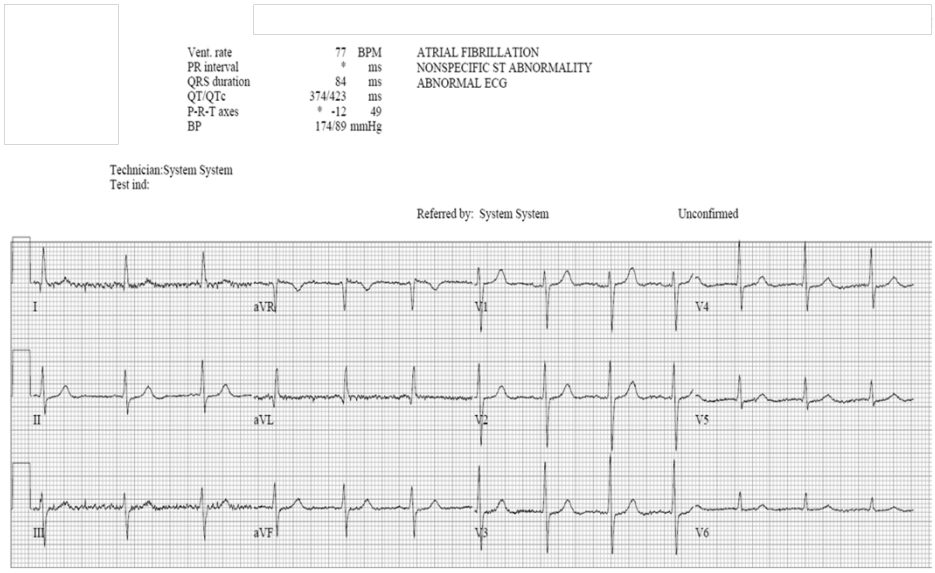
Atrial flutter

What is not Afib?



Sinus with premature atrial contractions

What is not Afib?

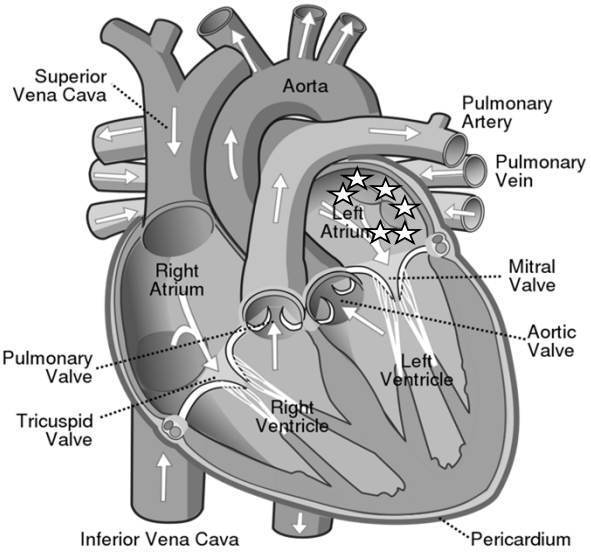


Sinus arrhythmia

AF Terminology

- **Paroxysmal Afib**
  Afib that terminates spontaneously or with intervention within 7 days of onset
- **Persistent Afib**
  Continuous Afib that is sustained for more than 7 days.
- **Long-standing persistent Afib**
  Continuous Afib more than 12 months in duration
- **Permanent Afib**
  Patient and clinician decide to stop further attempts to restore or maintain sinus rhythm
- **Non-valvular Afib (*Updated in 2019*)**
  Afib in the absence of moderate-to-severe mitral stenosis or mechanical heart valve
  Previous definition included rheumatic mitral stenosis, bioprosthetic or mechanical valve, mitral valve repair

Pathophysiology



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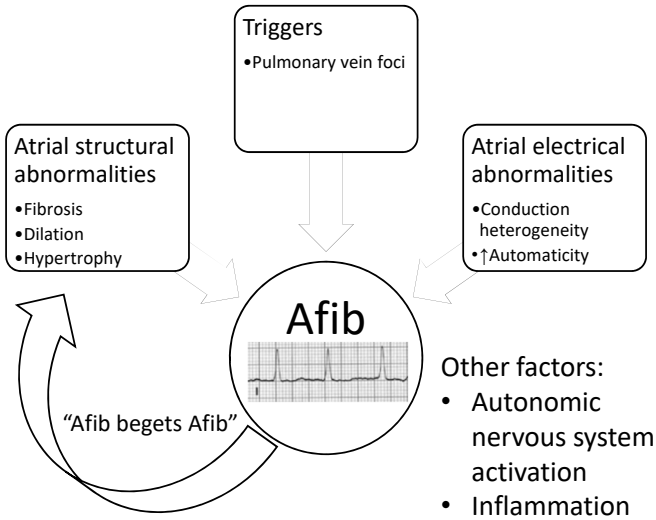


Other factors:
- Autonomic nervous system activation
- Inflammation
- RAAS activation

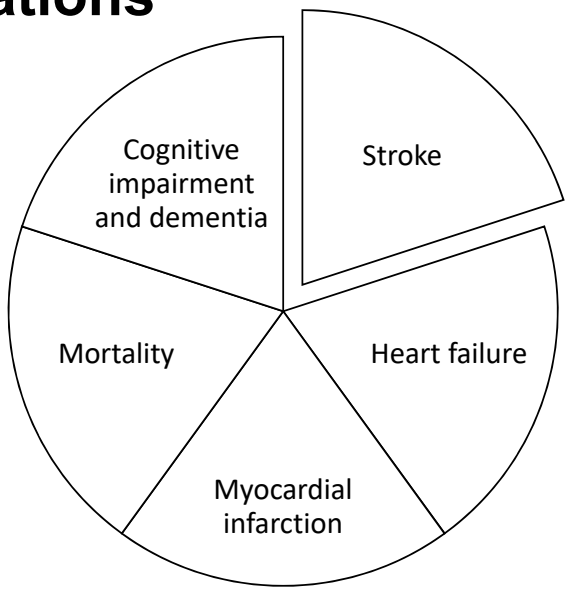
Risk factors for developing afib

Heart disease	Chronic conditions	Other factors
• Heart failure • Valvular disease • Coronary disease • HCM • Congenital heart disease	• Obesity • Hypertension • Diabetes • OSA • Hyperthyroidism • CKD	• Alcohol • Surgery • Infection • Inflammation • Genetics

Symptoms

- Palpitations
- Shortness of breath
- Chest discomfort
- Lightheadedness
- Weakness
- Fatigue
- Generalized malaise
- Heart failure symptoms
- Angina
- Syncope or near syncope
- No symptoms

Complications



Evaluation

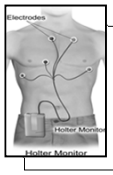
EKG
- Markers of other heart disease (LVH, ischemia)
- Pre-excitation
- QT interval (important for certain anti-arrhythmics)

Echo
- Assess LV function, valvular disease
- Left atrial size

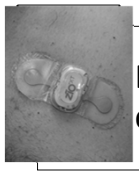
Labs
- Chemistry, CBC
- Thyroid function

Other
- Stress testing if signs of ischemia
- Sleep study if signs of OSA
- Ambulatory monitoring devices

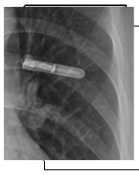
Monitoring devices



Holter monitor



Event monitor/mobile cardiac telemetry



Implantable loop recorder

Pacemaker/defibrillator

Personal devices

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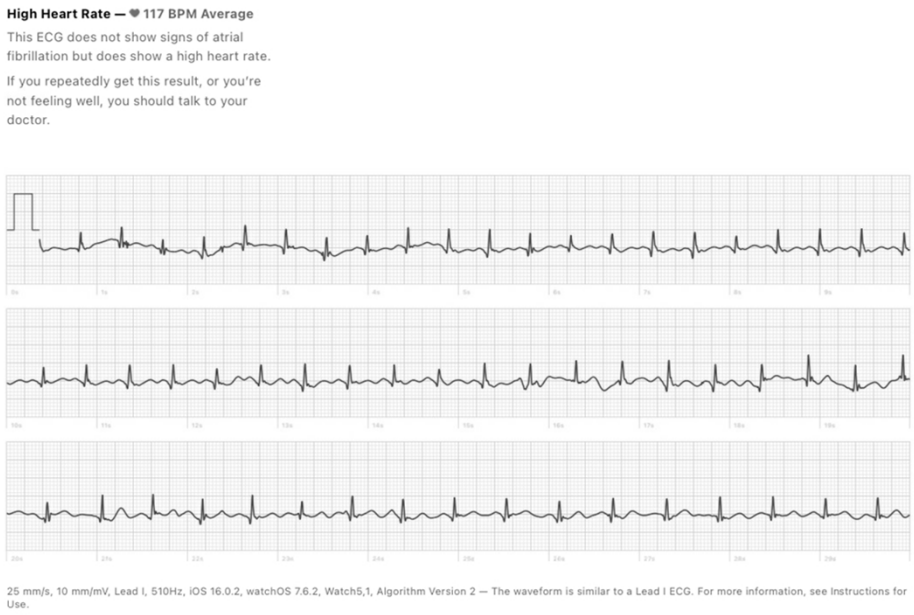
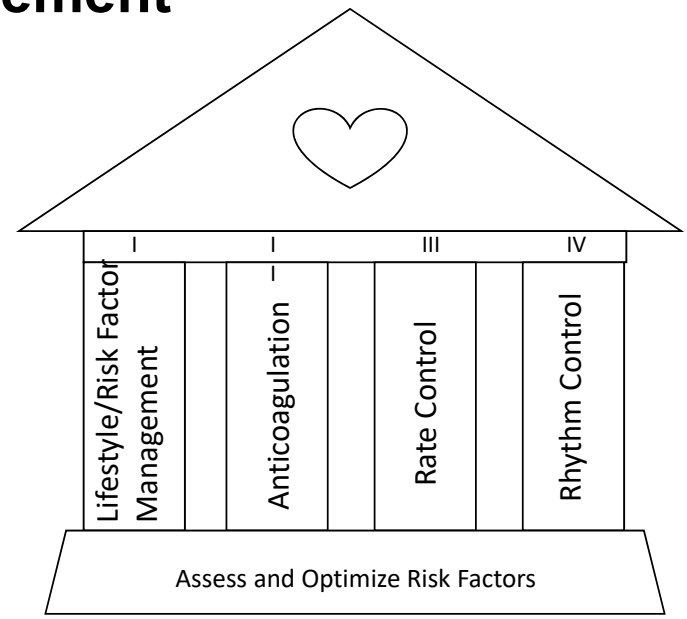
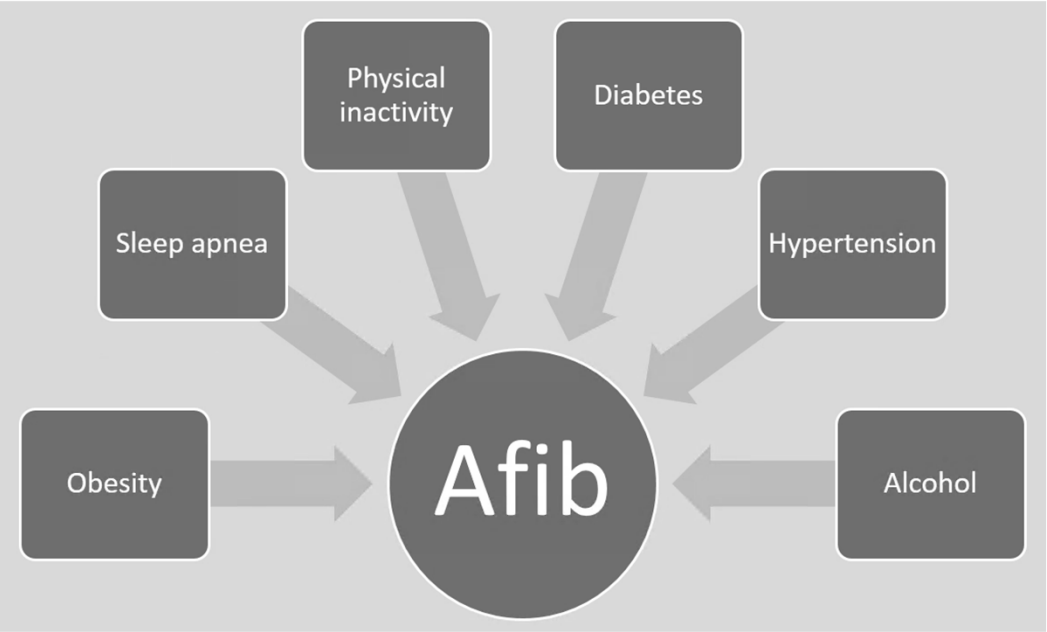
Monitoring devices



Management

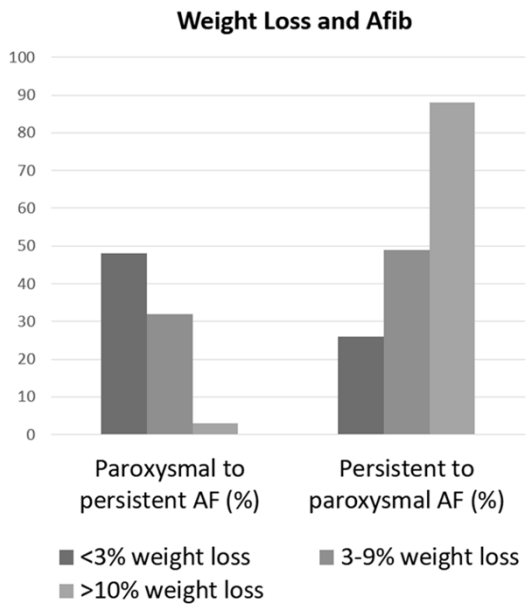


Lifestyle and risk factor modification



Obesity and Afib

- Obesity is a strong risk factor for Afib.
- Target a weight loss of at least 10% to help reduce Afib burden.
- Bariatric surgery in obese patients has been associated with reduced risk of new Afib and recurrence after ablation.
- For overweight and obese patients with Afib, weight loss combined with risk factor modification is recommended.



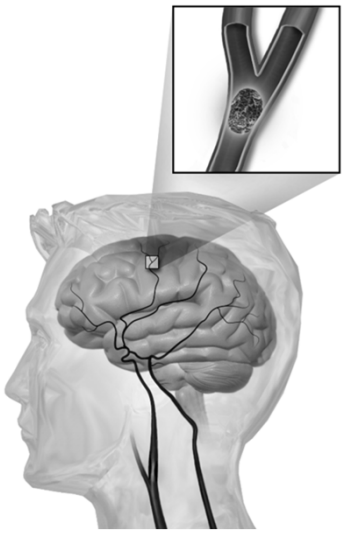
Circulation. 2020;141:e750–e772. DOI: 10.1161/CIR.0000000000000748

Lifestyle and risk factor modification

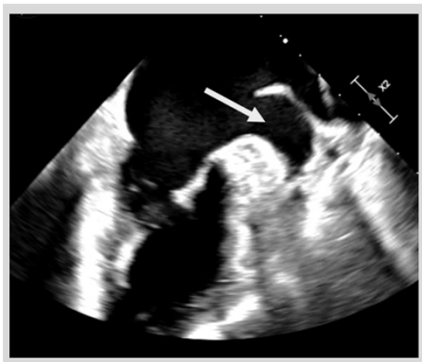
- **Physical Activity**
  - Increased physical activity (150min/week of moderate-intensity exercise) can help with prevention and treatment of Afib
- **Sleep Disordered Breathing**
  - Treatment of SDB may improve Afib burden
  - Screen and treat concomitant SDB in patients with Afib
- **Diabetes**
  - DM associated with higher risk for Afib
  - Glycemic control has been associated with reduced risk for Afib
- **Hypertension**
  - Hypertension associated with risk of developing Afib
- **Smoking**
  - Increases Afib risk. COPD is an independent risk factor.
  - Smoking negatively affects efficacy of Afib ablation
- **Alcohol**
  - >14 drinks/week significantly increased risk of Afib
  - Reduced alcohol consumption for patients with moderate to high levels of consumption

Stroke prevention

- Most frequent major complication of Afib
- Non-valvular Afib increases risk of stroke by 5x
- Greater risk for recurrent stroke, more severe disability, increased mortality
- Due to stasis of blood and reduced left atrial blood flow resulting in thrombus formation
- Left atrial appendage is most common location for thrombus formation
- Stroke risk is independent of Afib type (paroxysmal vs persistent vs permanent)

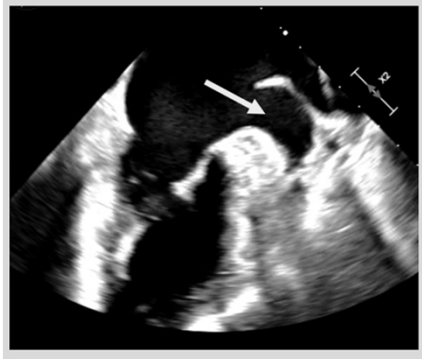


Left atrial appendage thrombus



Normal left atrial appendage

Left atrial appendage thrombus



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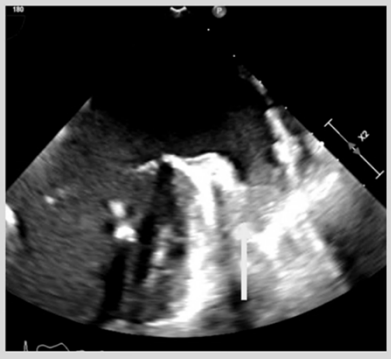
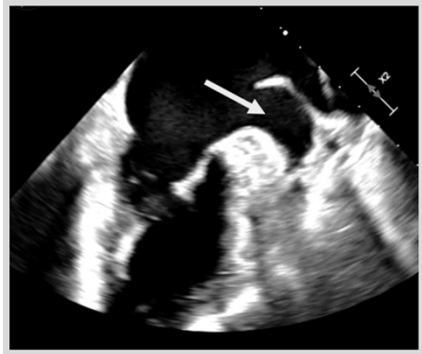


Dense spontaneous echo contrast with probable thrombus

Left atrial appendage thrombus



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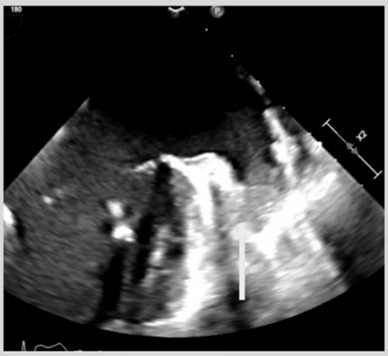

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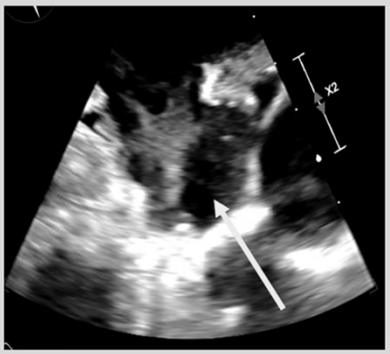
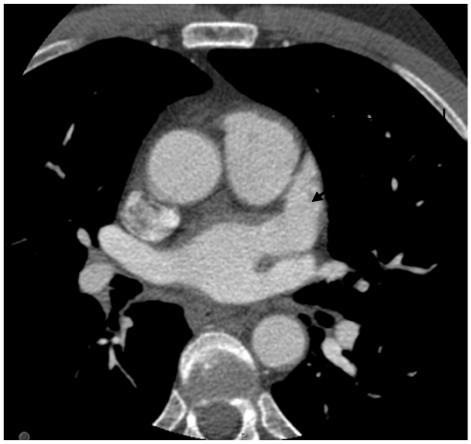


Left atrial appendage thrombus

Cardiac CT



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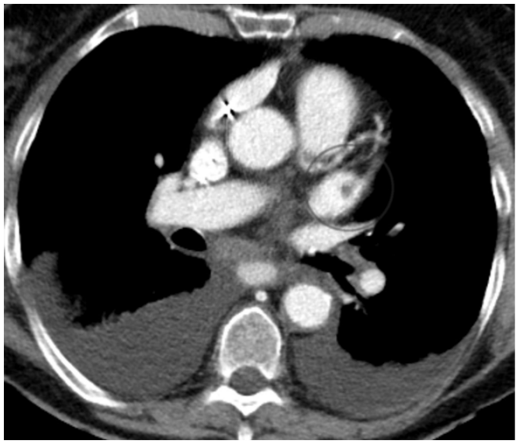


Left atrial appendage with thrombus

CHA_2DS_2VASc Score

CHA_2DS_2-VASc score is recommended for stroke risk assessment

Letter	Risk factor	Score
C	Congestive heart failure	1
H	Hypertension	1
A_2	Age ≥ 75	2
D	Diabetes	1
S_2	Stroke, TIA, thromboembolism	2
V	Vascular disease (myocardial infarction, peripheral arterial disease, aortic plaque)	1
A	Age 65-74	1
Sc	Sex category (female sex)	1

CHA_2DS_2VASc Score

- For patients with Afib and CHA_2DS_2VASc score ≥2 for men and ≥3 for women, oral anticoagulation is recommended. (*Update*)
- For patients with Afib and CHA_2DS_2VASc score of 1 for men and 2 for women, prescribing anticoagulant to reduce stroke risk may be considered.
- For patients with Afib and CHA_2DS_2VASc score of 0 for men and 1 for women, it is reasonable to omit anticoagulation.
- Selection of anticoagulant should be based on risk of thromboembolism, irrespective of whether Afib pattern is paroxysmal, persistent, or permanent.

CHA_2DS_2VASc Score	Annual Stroke Rate
0	0.2%
1	0.6%
2	2.2%
3	3.2%
4	4.8%
5	7.2%
6	9.7%
7	11.1%
8	11%
9	12.2%

Anticoagulants

- Choices include
  - Warfarin
  - Dabigatran
  - Rivaroxaban
  - Apixaban
  - Edoxaban

  } Non-vitamin K oral anticoagulants (NOACs) or direct-acting oral anticoagulants (DOACs)

- **DOACs are recommended over warfarin in Afib patients without moderate-to-severe mitral stenosis or a mechanical heart valve. (*Update*)**
- For patients with Afib who have mechanical heart valves, warfarin is recommended.
- For patients who are unable to maintain therapeutic INR, DOAC is recommended.

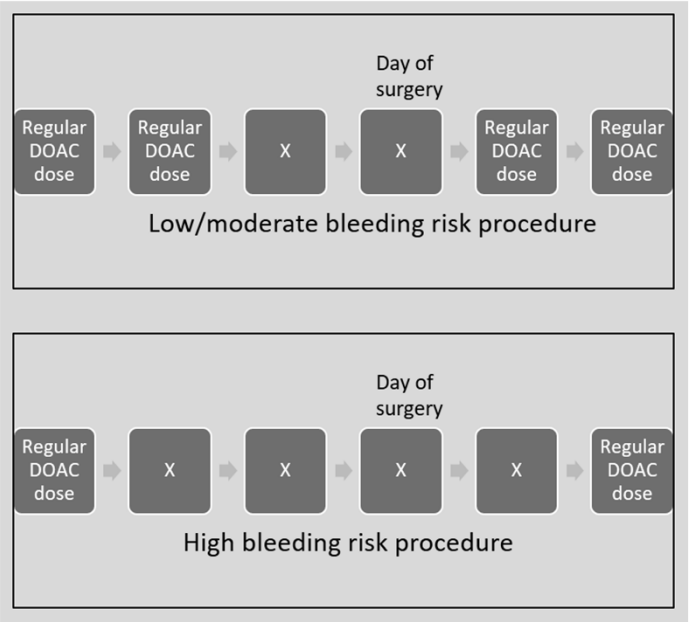
DOACs for Afib

	Mechanism	Comparison to warfarin	Kinetics	Dosing	Dosing adjustments	Reversal agent
Dabigatran	Direct thrombin inhibitor	110mg: stroke rates similar to warfarin, lower major hemorrhage 150mg: stroke rate lower than warfarin, similar major hemorrhage	$T^1/_2$ = 12-17hrs Peak effect 2hrs	150mg BID	- 75mg BID if CrCl 15-30 mL/min - Avoid use if CrCl <15 mL/min	- Idarucizumab - Prothrombin complex concentrate (PCC)
Rivaroxaban	Direct factor Xa inhibitor	Non-inferior to warfarin for stroke prevention, no difference in major bleeding, less frequent ICH and fatal bleeding	$T^1/_2$ = 5-9hrs Peak effect 3hrs	20mg daily with largest meal of day (evening)	- 15mg daily with evening meal if CrCl 15-50 mL/min - Avoid use if CrCl ≤15 mL/min	- Andexanet alfa - PCC
Apixaban	Direct factor Xa inhibitor	Superior to warfarin for stroke prevention, less bleeding and lower mortality	$T^1/_2$ = 12hrs Peak effect 3hrs	5mg BID	- 2.5mg BID if 2 of the following: age ≥80 yrs, body weight ≤60 kg, or serum Cr ≥1.5 mg/dL - No other adjustment for ESRD	- Andexanet alfa - PCC
Edoxaban	Direct factor Xa inhibitor	Non-inferior to warfarin for stroke prevention, lower rates of bleeding	$T^1/_2$ = 10-14hrs Peak effect 2hrs	60mg daily	- Avoid use if CrCl >95 mL/min - 30mg daily if CrCl 15-50 mL/min - Avoid use if CrCl <15 mL/min	PCC

Interruption and bridging

Patients on warfarin

- Bridging is recommended for patients with Afib and mechanical valve.
- For patients with Afib without mechanical valve:
  - Consider risks of stroke vs bleeding
  - Absence of bridging found to be non-inferior to bridging with LMWH and associated with decreased risk of bleeding
  - Bridging anticoagulation may be appropriate only for very high thromboembolic risk



What about aspirin?

- Anticoagulant ≠ Antithrombotic (anticoagulant & antiplatelet)
- "Anticoagulant" replaced "antithrombotic" in updated guidelines.
- Aspirin no longer recommended for stroke prevention in low risk patients.(*Update*)

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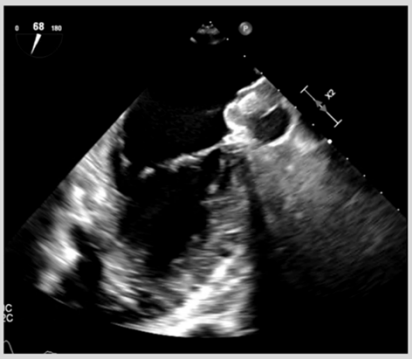
Non-pharmacologic stroke prevention

- Percutaneous left atrial appendage occlusion may be considered in patients at increased risk of stroke who have contraindications to long-term anticoagulation.(*Update*)
- Surgical occlusion/excision of the LAA may be considered in patients with Afib undergoing cardiac surgery.



WATCHMAN left atrial appendage occluder device

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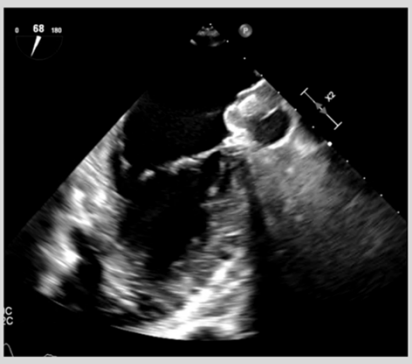

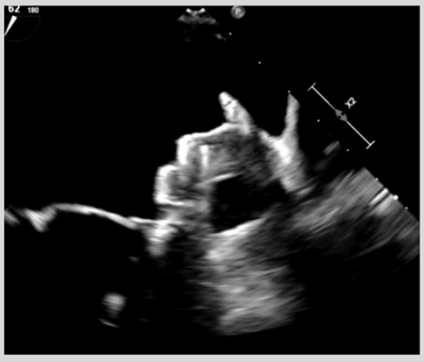

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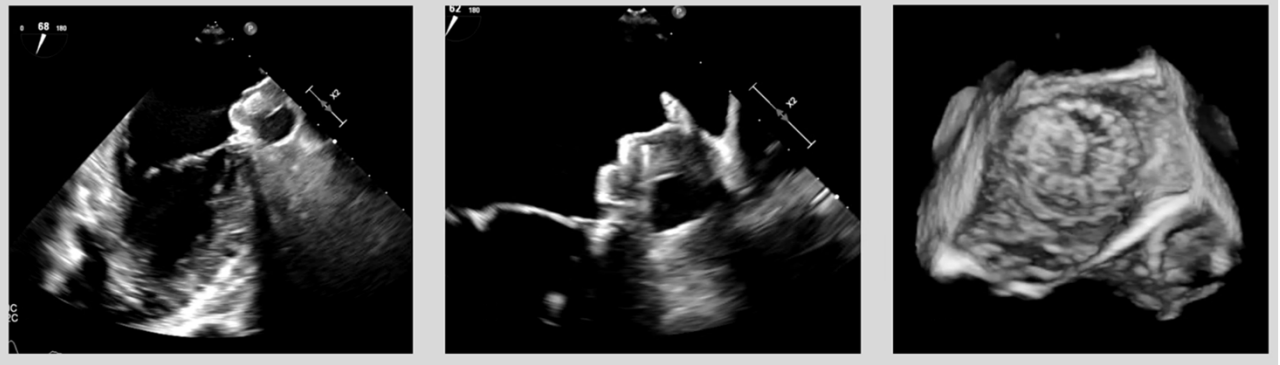

WATCHMAN left atrial appendage occluder device

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Salvatore J. Savona, MD, FACC
Clinical Assistant Professor
Cardiac Electrophysiology
Davis Heart and Lung Research Institute
The Ohio State University Wexner Medical Center

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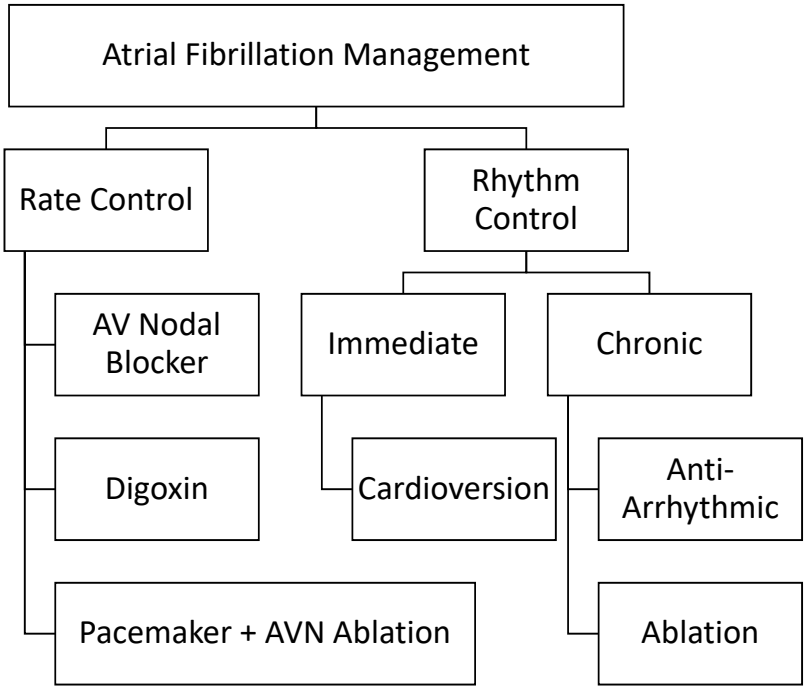
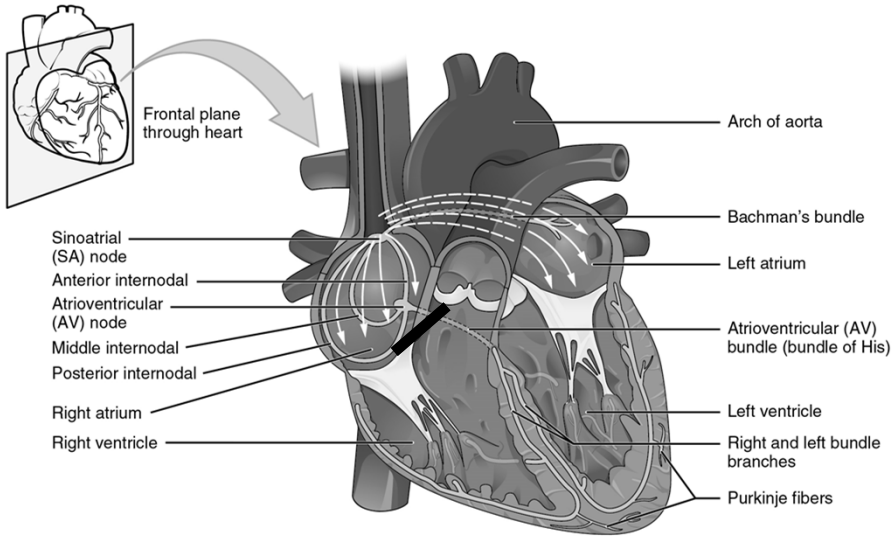
Left Atrial Appendage Closure

- **Candidates**
  - High risk for bleeding
  - Previous history of bleeding (major and non-major)
  - Non-compliant or labile INR
  - High risk lifestyle
- **Evaluation**
  - CHADSVASC ≥ 3
  - Suitable for anticoagulation
  - Appropriate candidate (above)
  - No other need for anticoagulation (mechanical valve, left ventricular thrombus, etc.)
- **Management**
  - Anticoagulation for 45 days followed by dual anti platelet therapy for 6 months
  - Chronic Aspirin therapy
  - Recently approved for dual anti platelet therapy only



Rate Control



Anterior view of frontal section

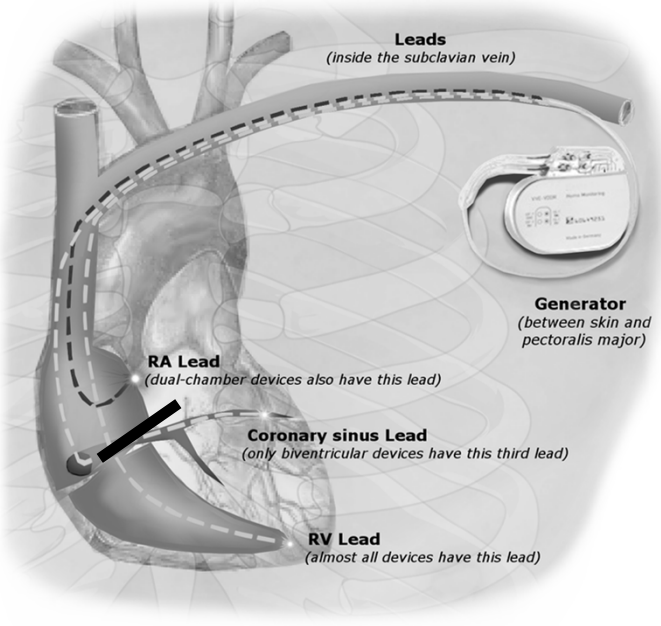
Anatomy & Physiology, Connexions Web site. http://cnx.org/content/col11496/1.6/, Jun 19, 2013.

Rate Control

- **Patient Population**
  - Permanent atrial fibrillation
  - Asymptomatic
  - Preserved LV function
- **Acute Management**
  - IV beta blocker or nondihydropyridine calcium channel blocker
  - Avoid nondihydropyridine calcium channel blocker in decompensated heart failure
- **Chronic HR Goal**
  - Resting heart rate < 80bpm
  - If asymptomatic and normal LV function, can consider a more lenient goal (<110bpm)

January, Craig T., et al. "2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 64.21 (2014): e1-e76.

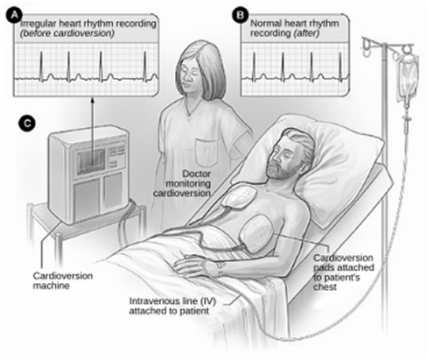
Class	Example	Mechanism	Side Effects
Beta Blocker	• Metoprolol • Carvedilol • Atenolol • Propranolol	Rate control achieved by inhibiting beta-1 receptors	• Depression • Erectile Dysfunction • Bradycardia • Fatigue
Nondyhdropyridine Calcium Channel Blocker	• Diltiazem • Verapamil	Inhibits calcium ion entry during depolarization	• Constipation • Lower Extremity Edema
Cardiac Glycoside	Digoxin	Suppression of AV node conduction via inhibition of Na/K ATPase -> increased intracellular Ca	• Too many to list • Requires drug level monitoring • Toxicity may require Digi-Fab



https://commons.wikimedia.org/wiki/File:PPM.png

Rhythm Control

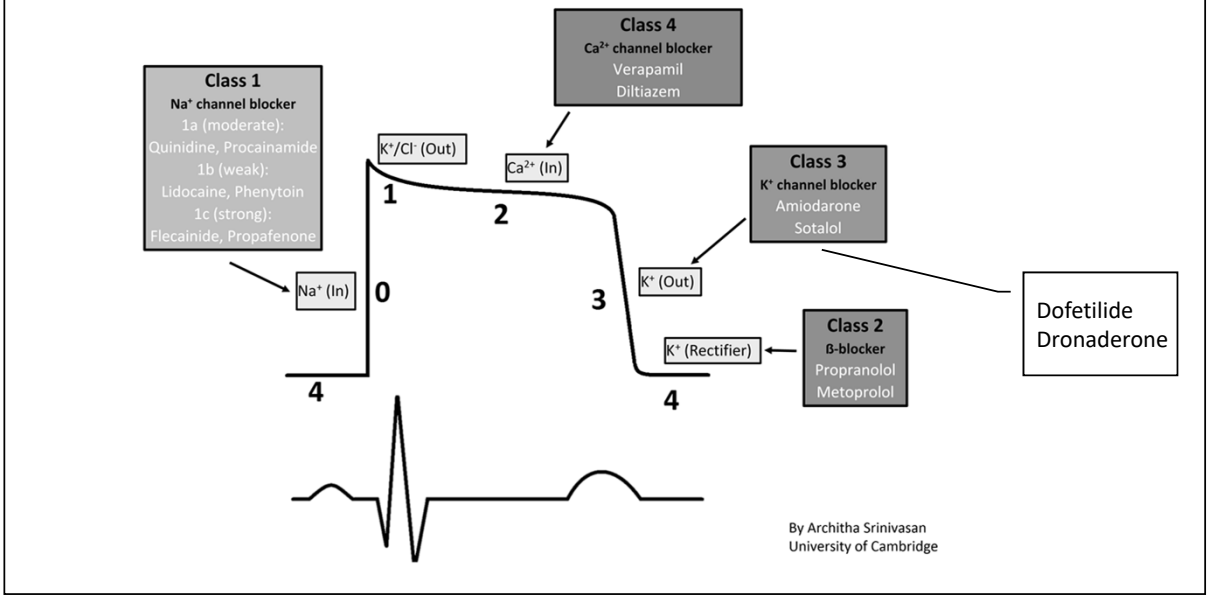
- **Patient Population**
  - Symptomatic
  - LV dysfunction and heat failure
  - Non permanent atrial fibrillation
- **Acute Management**
  - Electrical or chemical cardioversion
  - Prior to cardioversion
    - 3-4 weeks of uninterrupted anticoagulation regardless of CHADSVASC score or onset within 48 hours of cardioversion
    - Transesophageal echo or CT pulmonary vein showing no left atrial or left atrial appendage thrombus
  - Following Cardioversion
    - 4 weeks of uninterrupted anticoagulation, regardless of CHADSVASC score



- https://commons.wikimedia.org/wiki/File:Cardioversion.svg

- January, Craig T., et al. "2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society." *Journal of the American College of Cardiology* 64.21 (2014): e1-e76.

Drugs Affecting the Cardiac Action Potential



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Antiarrhythmic Maintenance of Sinus Rhythm

Class	Mechanism	Drug	Monitoring	Contraindications	Notes
1c	Na Channel Blockade	- Flecainide - Propafenone	- Baseline ECG Stress Test - Renal and Liver	- Structural heart disease - Conduction disease	**Must** be taking with an AV nodal blocking agent
III	K Channel Blockade	- Sotalol - Dofetilide - Dronaderone	- QT/QTc - Renal Function	- ESRD - Prolonged QT - Bradyarrhythmia	Do not use dronaderone in symptomatic heart failure, NYHA IV or permanent AF
Many	Na, K, CCB, and BB	Amiodarone	- Thyroid - Liver - Pulmonary (CXR and DLCO)	- Pulmonary and liver disease - Hyperthyroid - Heart block - Iodine hypersensitivity	- Photosensitivity - Ocular and neurologic involvement

Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Trial

- 2002 in New England Journal of Medicine
- Compared mortality in rate vs rhythm control strategy in ~4000 patients
- Majority of rate control- beta blocker and digoxin
- Majority of rhythm control- amiodarone and sotalol
- Higher incidence in rhythm control:
  - pulmonary event (7.3 vs 1.3)
  - gastrointestinal event (8.0 vs 2.1)
  - bradycardia (6.0 vs. 4.2)
  - prolonged QTc (1.9 vs 0.3)
- Conclusion- “Management of atrial fibrillation with the rhythm-control strategy offers no survival advantage over the rate-control strategy, and there are potential advantages, such as a lower risk of adverse drug effects, with the rate-control strategy”

Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. "A comparison of rate control and rhythm control in patients with atrial fibrillation." *New England Journal of Medicine* 347.23 (2002): 1825-1833.

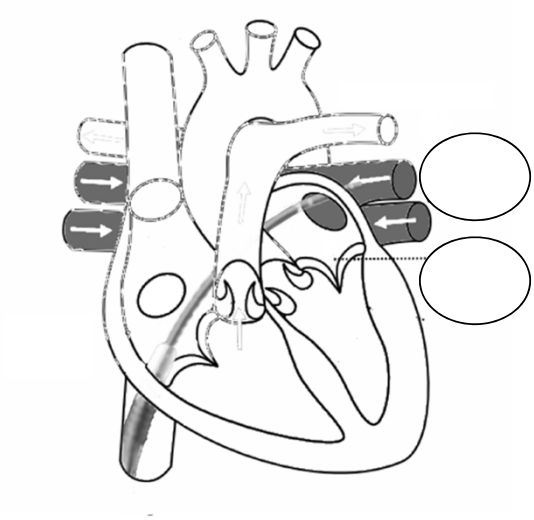
Why Choose Rhythm Control?

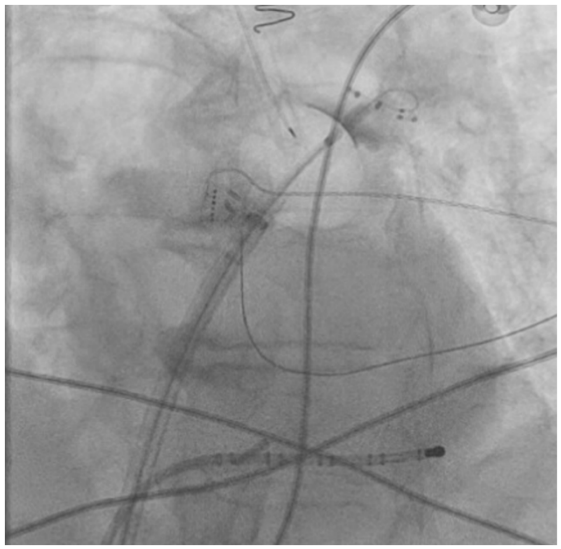
- Much has changed since 2002
- Only 14 patients received an AF ablation
- Therapeutic INR in only 62.3%

- **Follow-up Analysis**
  - 5 year follow-up showed a greater risk of heart failure in rate control strategy (21.4% vs 16.4%)
  - Increase in total mortality (HR 2.83), cardiac mortality (4.27) and hospitalization (HR 3.04)
  - Risk factors for heart failure
    - Rate >80 bpm
    - AF burden, especially >75%

- Slee A, Saksena S. Impact of initial heart failure emergence on clinical outcomes of atrial fibrillation patients in the AFFIRM trial. Am Heart J. 2020 Feb;220:1-11. doi: 10.1016/j.ahj.2019.10.005. Epub 2019 Oct 28. PMID: 31756389.
- Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. "A comparison of rate control and rhythm control in patients with atrial fibrillation." *New England Journal of Medicine* 347.23 (2002): 1825-1833.
- https://commons.wikimedia.org/wiki/File:2016_Fiat_Ducato_42_Maxi_West_Midlands_Ambulance_Service_3.0.jpg

Atrial Fibrillation Ablation





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Ablation Outcomes

- **Mortality**
  - CABANA: No difference in all cause mortality. Improvement in hospitalization and AF recurrence
  - CASTLE-AF: Significant improvement in mortality in systolic heart failure (HR 0.56)
- **Timing**
  - EAST-AFNET 4: early rhythm control resulted in reduction of stroke by 1/3 and total mortality reduced by 16%
- **Symptoms**
  - STOP AF: Improvement in symptoms with ablation (54%) vs AAD (29%)

- Packer DL, Mark DB, Robb RA, et al. Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial. *JAMA*. 2019;321(13):1261–1274. doi:10.1001/jama.2019.0693
- Marrouche, Nassir F., et al. "Catheter ablation for atrial fibrillation with heart failure." *New England Journal of Medicine* 378.5 (2018): 417-427.
- Kirchhof, Paulus, et al. "Early rhythm-control therapy in patients with atrial fibrillation." New England Journal of Medicine 383.14 (2020): 1305-1316.
- Wazni, Oussama M., et al. "Cryoballoon ablation as initial therapy for atrial fibrillation." *New England Journal of Medicine* 384.4 (2021): 316-324.

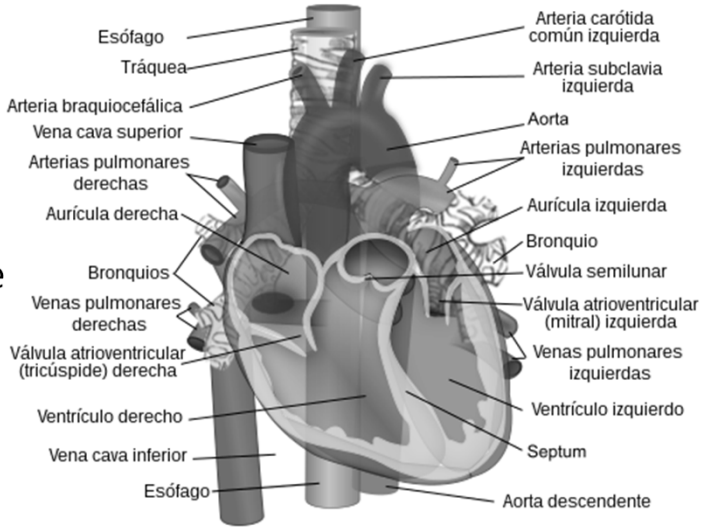
Safety of Ablation- CABANA

	Ablation (n=1108)	Drug Therapy (n=1096)
Death	58 (5.2)	67 (6.1)
Disabling Stroke	3 (0.3)	7 (0.6)
Serious Bleeding	36 (3.2)	36 (3.3)
Cardiac Arrest	7 (0.6)	11 (1.0)

- Packer DL, Mark DB, Robb RA, et al. Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial. *JAMA*. 2019;321(13):1261–1274. doi:10.1001/jama.2019.0693

On the Horizon- Pulsed Field Ablation

- Electroporation through direct current pulses
- Rapid ablation potential
- Initial data is supportive of low risk for collateral damage
  - Esophagus
  - Phrenic nerve
  - Coronary artery?
  - Pericardial effusion



https://commons.wikimedia.org/wiki/File:Relations_of_the_aorta,_trachea,_esophagus_and_other_heart_structures-es.svg

Conclusions

- Atrial fibrillation remains a significant burden for patients and the medical system
- Appropriate prevention of stroke based on risk factors is of utmost importance
- Risk factor modification can have a significant improvement in atrial fibrillation burden
- Rhythm control options, especially early in the course of disease can reduce the burden of disease and improve outcomes
- Ablation therapy is safe and efficacious, with a larger role in the management of atrial fibrillation