Fickle Flutterings

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Objectives

- Review the burden, risk factors, and pathophysiology of atrial fibrillation
- Go over classification and anticoagulation
- Treatment and medications
- Special populations to consider

Pre Test Questions- Question 1

65 y/o gentleman with a past medical history of HTN, DM II, and an MI 3 years ago who presents to your office with complaints of palpitations for the past 12 hours. You do an EKG and find that he is in atrial fibrillation. He refuses to undergo a transesophageal echocardiogram before the test.

What is the minimum amount of time he should be on anticoagulation before your cardiovert him?

How long to anticoagulate?

A) 1 week
B) 2 weeks
C) 3 weeks
D) 4 weeks

Pre Test Question 2

The same gentleman gets successfully cardioverted! You now decide that he will require medication to stay in normal sinus rhythm. His past medical history includes HTN, CAD, and DM II. His EKG in normal sinus rhythm is unremarkable.

What medication is not allowed in this patient?

Which medication should you avoid?

A) Metoprolol Succinate

B) Digoxin

C) Dofetilide

D) Flecanide

Pre Test Question 3

You are taking care of 75 y/o F with permanent atrial fibrillation, diabetes, HTN, CAD, and ESRD on MWF dialysis. She has no real complaints but you draw her INR today and you find that it is 1.7. When you review the chart, you find that is frequently subtherapeutic over the last 6 months. You discuss this with her and she says that she has a new found love of leafy vegetables.

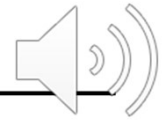
What anticoagulant can be considered?

What anticoagulant?

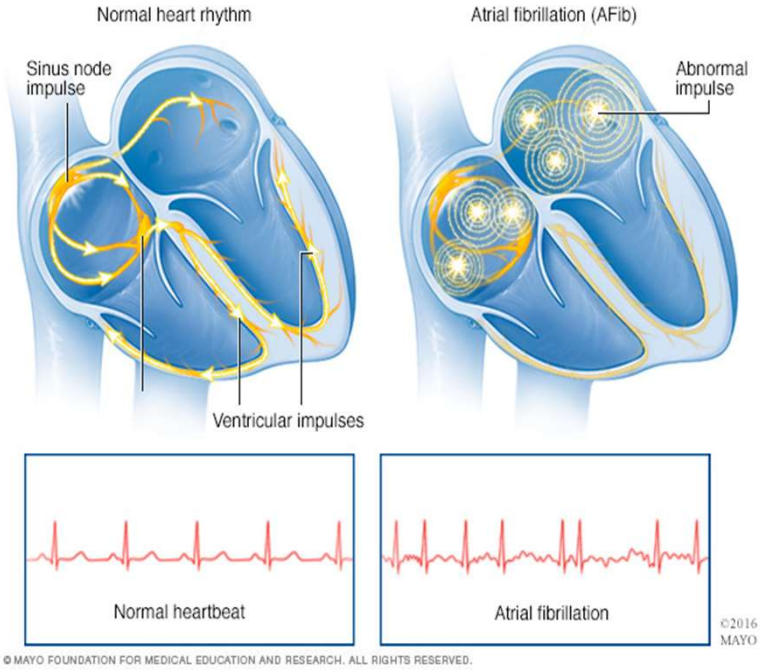
A) Dabigitran
B) Apixaban
C) Rivoraxaban
D) Endoxaban

Disclosures

- None



What is atrial fibrillation?



Atrial Fibrillation is a supraventricular tachycardia with uncontrolled atrial activity causing ineffective atrial contraction.

Burden of Atrial Fibrillation

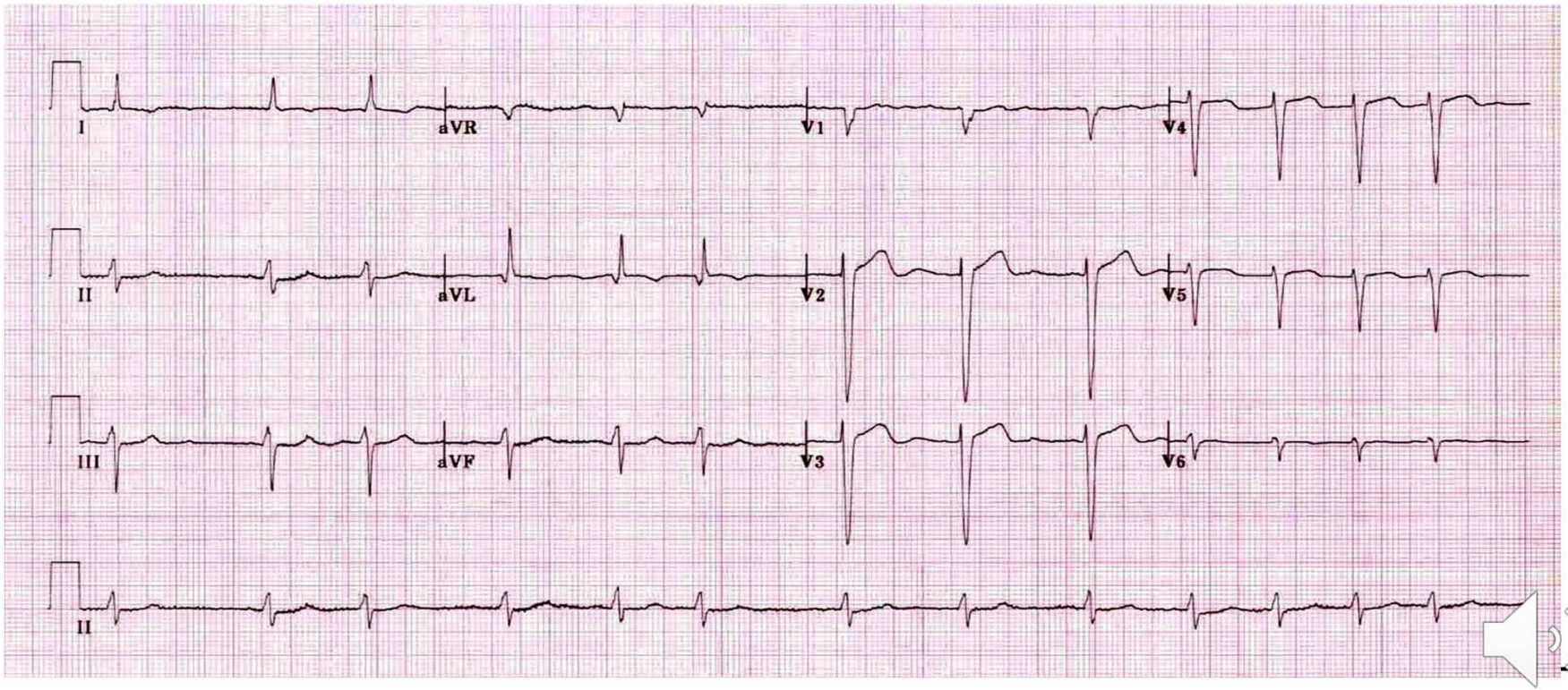
Most common abnormal heart rhythm in the general population.

1-2% of the general population below the age of 65.
9% of the population above the age of 65.

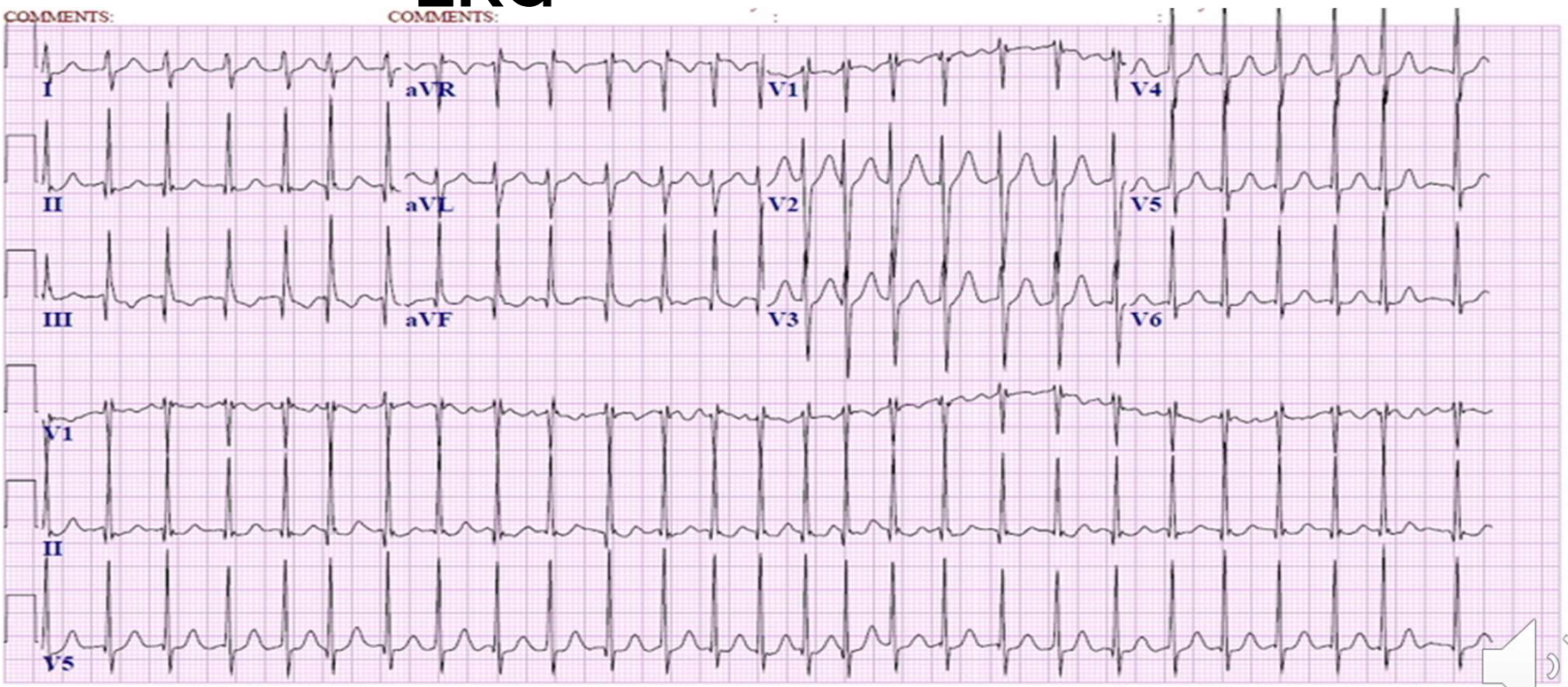
Medical Costs for a patient with atrial fibrillation is $8,700 higher than patients without a-fib. Total cost to the US is about 26 billion dollars.

It's only going to get worse.

EKG



EKG



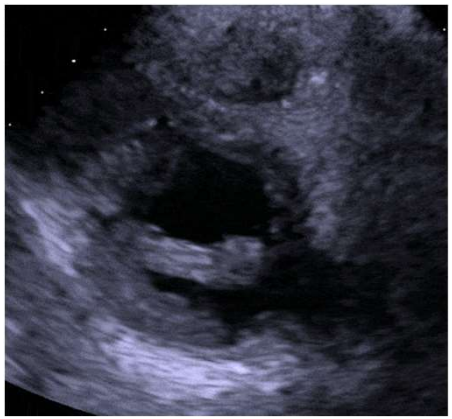
Classification

Paroxysmal: Atrial Fibrillation lasting less than 7 days

Persistent: Atrial Fibrillation lasting more than 7 days

Long Standing Persistent: Continuous Atrial Fibrillation lasting more than 12 months

Permanent: A decision made by the patient and the physician to no longer pursue sinus rhythm



Valvular vs Non-Valvular

This term is no longer recommended per 2019 guidelines.

Valvular: Atrial fibrillation that is associated with moderate to severe MS or mechanical valve replacement.

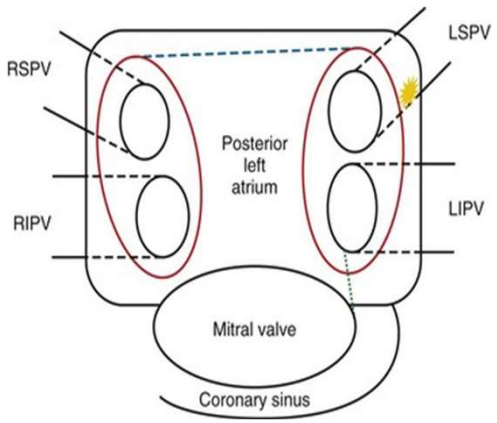
Non-valvular: Absence of moderate to severe MS or mechanical valve replacement.

Pathophysiology

Atrial fibrillation consists of multiple reentrant circuits that do not cause adequate atrial contraction. Potential triggers include

Parasympathetic/Sympathetic
Tachycardia/Bradycardia
Accessory AV pathways
Atrial Stretch
EtOH (Holiday Heart)
Drugs
Ectopic foci in the pulmonary veins
Surgery
Obstructive Sleep Apnea

Pathophysiology



In paroxysmal atrial fibrillation, it is usually caused by a trigger from the pulmonary veins.

- **The pulmonary veins have been found to contain P cells (normally found in the AV and SA nodes and initiate propagation), purjinke fibers (conduction cells in the ventricle), and transitional cells.**
- **Most of these are remnants from our embryologic development.**

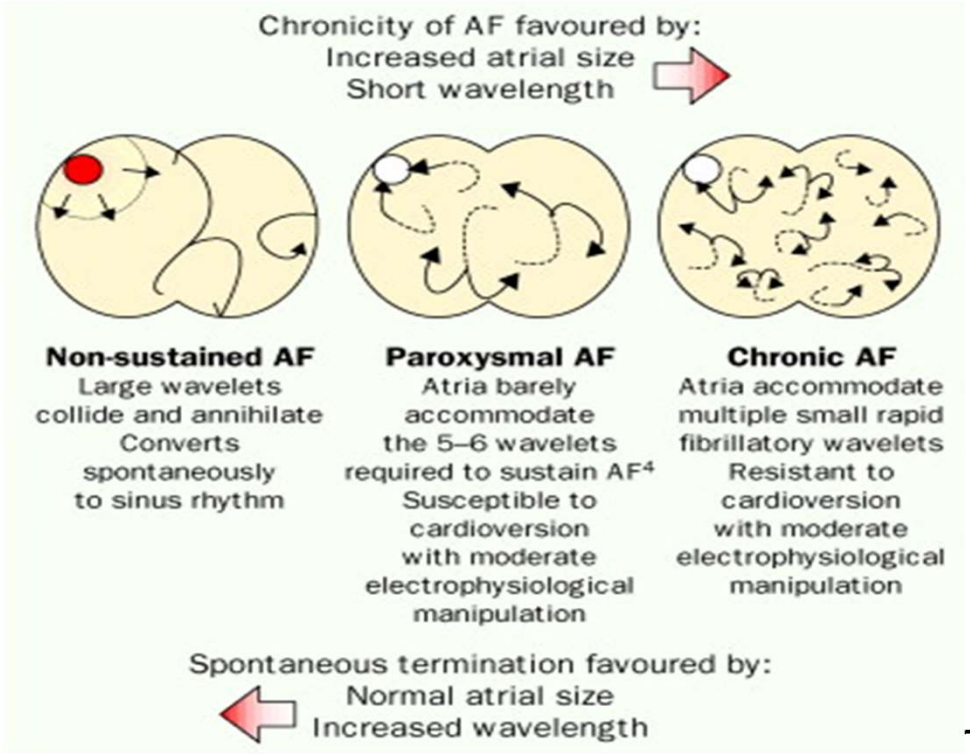
In persistent atrial fibrillation, it usually is the atrial remodeling/scarring that is driving the atrial fibrillation

Pathophysiology- Propagation

Once atrial fibrillation is started, what keeps it going?

The wavelet and rotor theory

Wavelets and Rotors



Wavelets and Rotors

Paroxysmal Atrial Fibrillation

Wavelets have a wide diameter and the atrium can only accommodate a few wavelets.

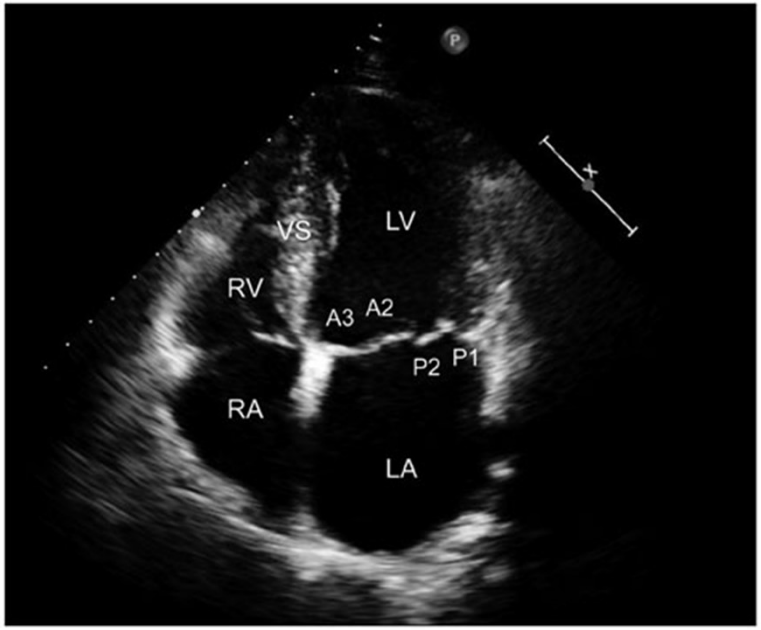
Persistent Atrial Fibrillation

Wavelets diameter decreases increases the number of wavelets and rotors in the atrium. Atrium starts to enlarge.

Permanent Atrial Fibrillation

Wavelets decrease and number of rotors increase. Atrium is very enlarged.

Pathophysiology- Atrial Enlargement



“A heart in atrial fibrillation wants to stay in atrial fibrillation. The heart in normal sinus rhythm wants to stay in normal sinus rhythm”

-Dr Solomon

Risk Factors

Age

Hypertension

Heart Failure

Valvular Disease

Coronary Artery Disease

Hyperthyroidism

Obstructive Sleep Apnea

Electrolyte Disorders

Alcohol (Holiday Heart)

Pulmonary Disease

Obesity

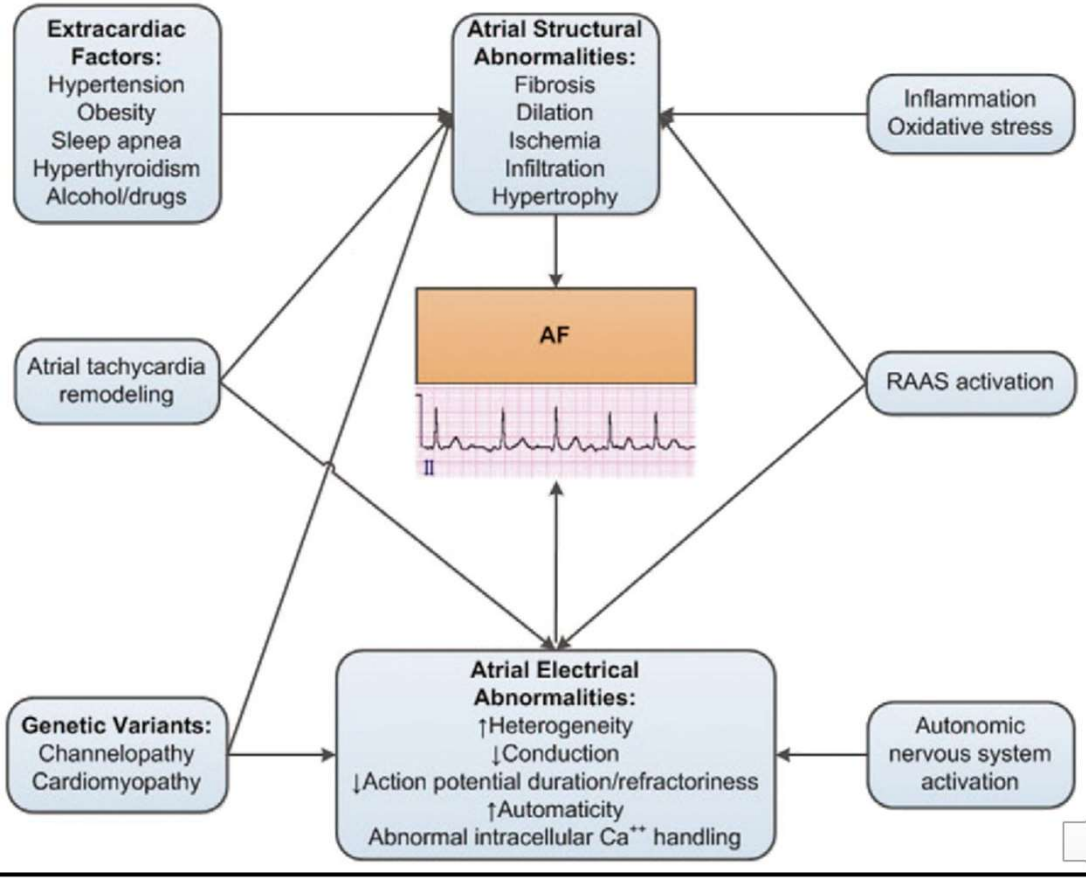
Rheumatic Heart Disease

Male Sex

Risk Factors

What do all of these risk factors have in common?
They all can cause

- **Atrial Fibrosis**
- **Dilation**
- **Ischemia**
- **Infiltration**
- **Hypertrophy**


Extracardiac Factors:
Hypertension
Obesity
Sleep apnea
Hyperthyroidism
Alcohol/drugs
Atrial Structural Abnormalities:
Fibrosis
Dilation
Ischemia
Infiltration
Hypertrophy
Inflammation
Oxidative stress
AF
Atrial tachycardia remodeling
RAAS activation
II
Genetic Variants:
Channelopathy
Cardiomyopathy
Atrial Electrical Abnormalities:
↑Heterogeneity
↓Conduction
↓Action potential duration/refractoriness
↑Automaticity
Abnormal intracellular Ca++ handling
Autonomic nervous system activation

Presentation

Asymptomatic

Fatigue

Dyspnea on exertion

Palpitations

Stroke

Hemodynamic Instability

Complications

Stroke

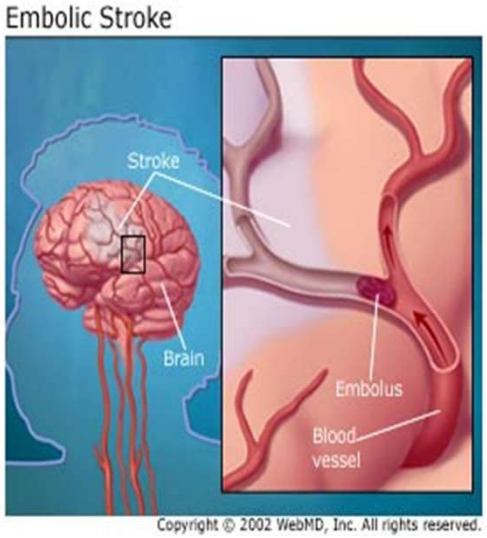
Cardiac Decompensation

Tachy-induced cardiomyopathy

Palpitations

Loss of energy

Stroke



Stroke is one of the most serious and common complications of atrial fibrillation.

Strokes from atrial fibrillation have worse neurological outcomes and don't have the same degree of recovery.

Stroke

Patients with atrial fibrillation have been known to have an increased risk in stroke since the 1980s.

In the 1990s, the Stroke Prevention in Atrial Fibrillation (SPAF) looked at warfarin vs aspirin vs placebo

SPAF and subsequent trials showed warfarin reduced the chances of developing a stroke by 67%.

Who do we anticoagulate?

CHA2DS2VASc

C= Congestive Heart Failure
H= Hypertension
A= Age greater than 75 (2 points)
D= Diabetes
S= Stroke/TIA/Thromboembolism (2 points)
V= Vascular Disease (PAD, MI, or aortic plaque)
A= Age between 65-74
Sc= Sex Category (Female =1, Male =0)

CHA2DS2VASc

Score	Chance of Stroke
0	0%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	12.5%
9	15.2%

CHA2DS2VASc

At what score do you anticoagulate?

0-1= No anticoagulation
Males: 2+= Anticoagulate
Females: 3+= Anticoagulate

Anticoagulation

Vitamin K Inhibitors

Warfarin/Coumadin

NOAC

Rivoraxoban (Xarelto)- Factor Xa Inhibitor

Apixiban (Eliquis)- Factor Xa Inhibitor

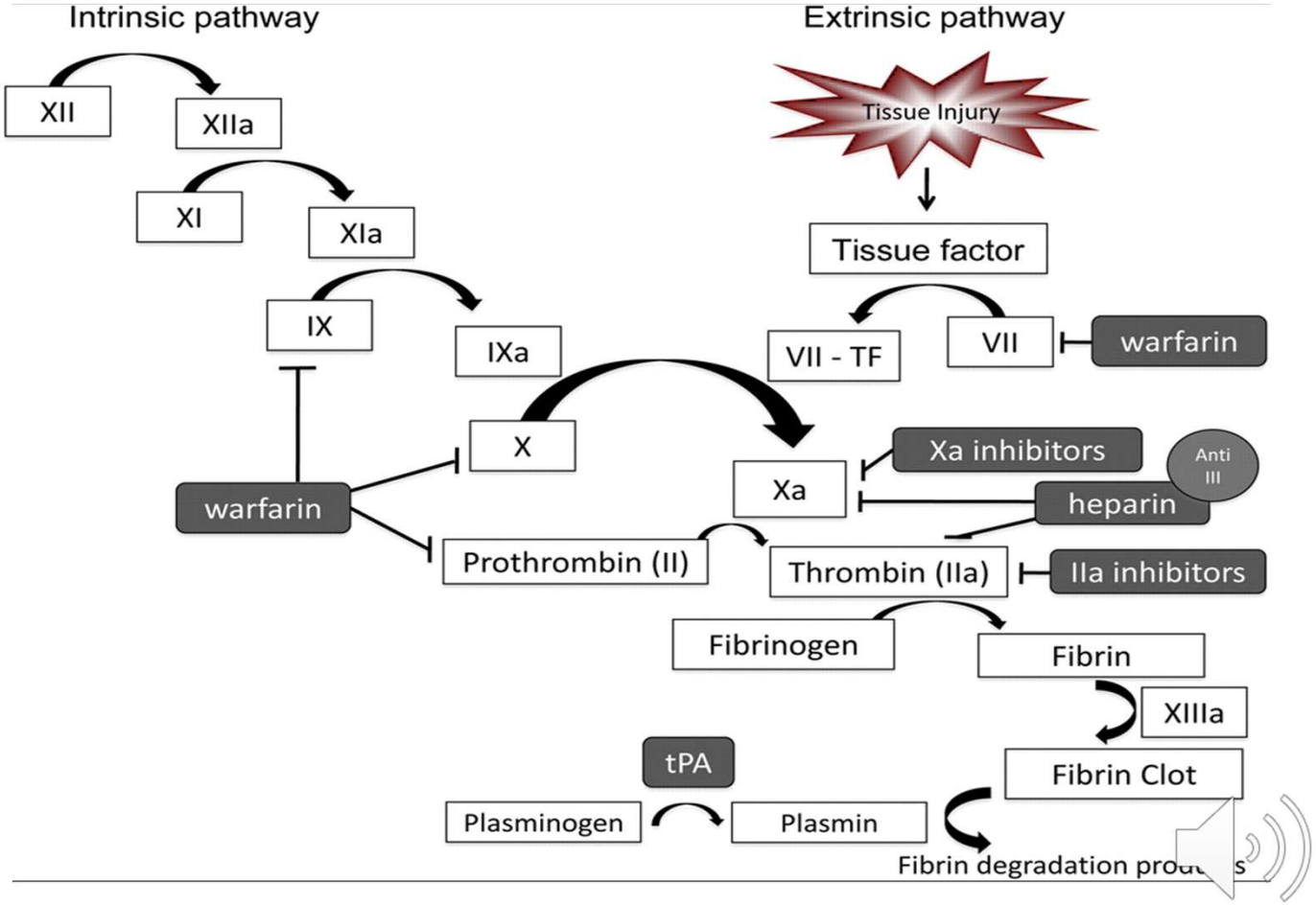
Dabigatran (Pradaxa)- Direct Thrombin Inhibitor

Edoxaban (Savaysa)- Factor Xa Inhibitor

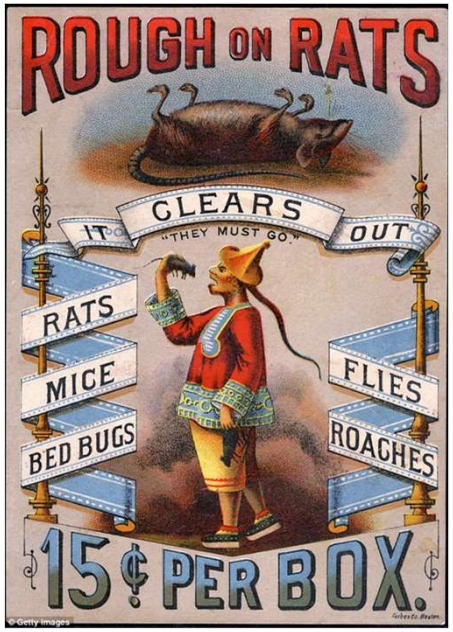
Antiplatelet

ASA 81mg

ASA 81 mg + Plavix


Intrinsic pathway
Extrinsic pathway
XII
XIIa
XI
XIa
IX
IXa
X
Tissue Injury
Tissue factor
VII - TF
VII
warfarin
Xa inhibitors
Anti III
Xa
heparin
warfarin
Prothrombin (II)
Thrombin (IIa)
IIa inhibitors
Fibrinogen
Fibrin
XIIIa
Fibrin Clot
tPA
Plasminogen
Plasmin
Fibrin degradation products

Anticoagulants- VKI



Warfarin (Coumadin and Jantoven)

Dosing: Variable

Pros: Longest studied and most well known drug. Approved for all cases of atrial fibrillation; cheap; reversible.

Cons: Needs frequent monitoring (weekly during initiation or changes and then monthly there after); INR affected by diet; multiple drug interactions

Other indications: DVT/PE prophylaxis and treatment. LV thrombus. Multiple coagulation disorders

Anticoagulants- NOAC

Factor Xa Inhibitors

Rivoroxaban (Xarelto)

Apixiban (Eliquis)

Edoxaban (Savaysa)

Direct Thrombin Inhibitor

Dabigitran (Pradaxa)

NOAC Indications

Atrial fibrillation except for atrial fibrillation with mitral stenosis or mechanical valve

Deep Vein Thrombosis prophylaxis and treatment

Pulmonary Embolism treatment

Factor Xa Inhibitors- Apixaban

Dosing: 5 mg BID. 2.5 mg if patient meets ⅔ of the following: creat > 1.5, 80 or older, and weight < 60 kg

ARISTOLE: Showed that Eliquis was SUPERIOR to Warfarin. Compared to warfarin, Eliquis reduces stroke by 21%, major bleeding by 31%, and mortality by 11%

Pro: Lowest bleeding risk; no problems with diet. Class IIb indications for patients with ESRD

Con: Twice a day dosing.

Factor Xa Inhibitors- Rivaroxaban

Dosing: 20 mg qd. CrCl 15-50 reduce to 15 mg qd.

ROCKET AF: Showed that Xarelto was non-inferior to warfarin without any increase in bleeding events.

Pros: Once daily dosing.

Cons: Must be taking with fattiest meal of the day

Additional indications: Chronic CAD/PAD (2.5 mg BID + baby aspirin)

Factor Xa Inhibitor- Savysa

Dosing: 60 mg qd for CrCl 50-95. CrCl 15-50 reduce to 30 mg qd.

ENGAGE-AF: Showed that Endoxaban was superior to warfarin without any increase in bleeding events.

Pros: Once daily dosing.

Cons: Need to monitor renal function for dosing

Direct Thrombin Inhibitor- Dabigitran

Dosing: 150 mg BID. CrCl 15-30 75 mg BID.

RELY-AF: non-inferior to warfarin without any significant increase in bleeding events.

Pros: Longest approved NOAC.

Cons: Twice a day dosing

Antiplatelets for anticoagulation

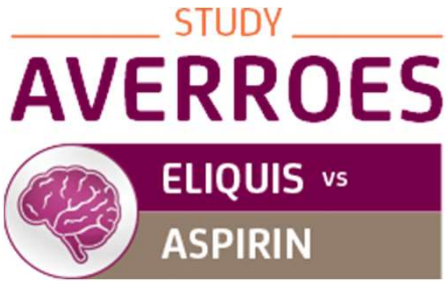
ACTIVE Trial

- **Plavix 75 mg and low dose aspirin in patient's that were unable to receive vitamin K antagonist.**
- **Although aspirin and plavix was better than aspirin alone, you also had a significant increase in hemorrhagic (mostly GI) bleeding.**

SPAF II

- **Looked at Warfarin vs ASA 325 mg**
- **In younger patients without risk factors, Warfarin was superior to aspirin but the relative risk reduction was small**

AVERROES Trial

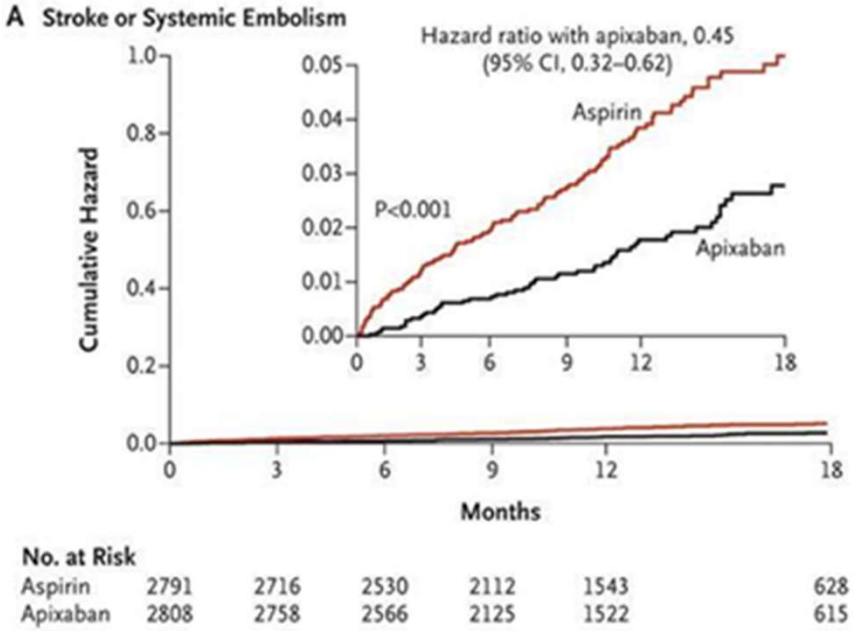


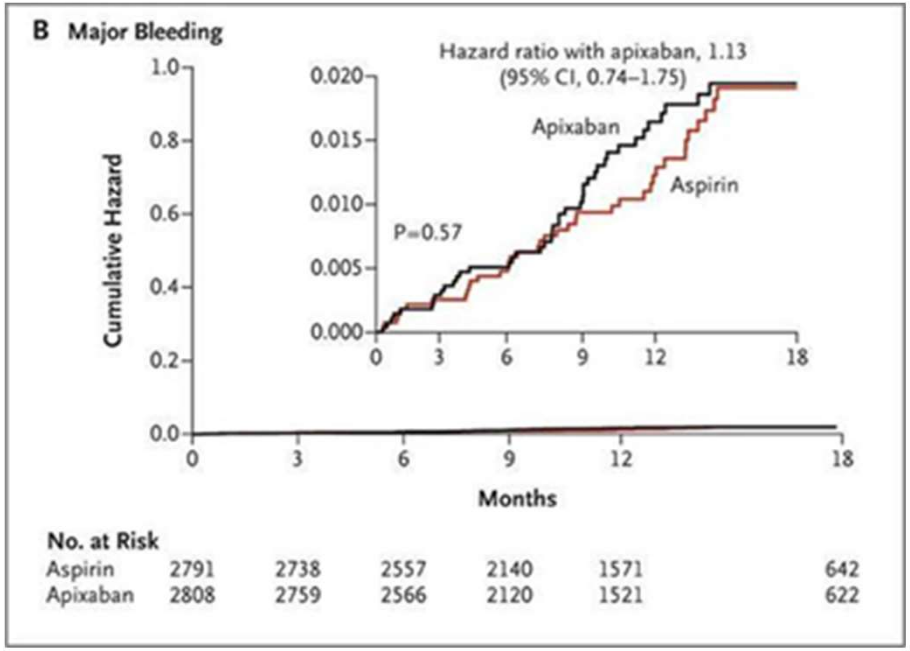
Studied patients that were thought to be unsuitable for coumadin and placed them on ASA 81 mg vs Eliquis 5 mg.

Study was stopped after a year due to a significant decreased rate of stroke (1.6%/year for Eliquis and 3.7%/year for ASA) without any significant increase in major bleeding events (1.4%/year for Elqiuis vs 1.2%/year for Aspirin).

Eliquis was also better tolerated than aspirin.

AVERROES Trial





CHA2DS2VASc Score of 1 or 2

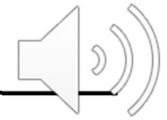
AVVEROES Trial showed apixaban was better tolerated and had fewer major bleeding events when compared to aspirin.

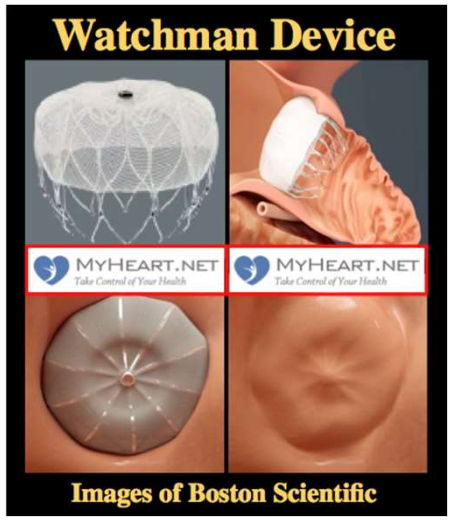
No increase in hemorrhagic events when Eliquis was compared to aspirin.

Risk of stroke w/ apixaban was significantly lower than with aspirin alone.

Left Atrial Appendage Occlusion Device

- **Watchmen is currently the only one that is approved by the FDA**
- **Amplatzer Amulet is currently going through clinical trials for approval by the FDA. Currently approved internationally.**

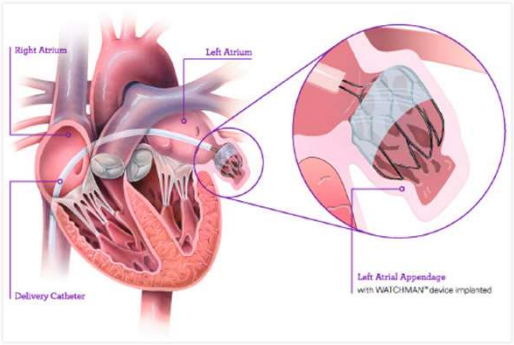




Watchmen Device

Inserted for patients that have bleeding complications and can't be anti-coagulated.

Interventional cardiology procedure that is done through the groin.



Overtime, the device endothelioses completely covering the left atrial appendage.

Watchmen Device- Anticoagulation

Post Device Implantation Anticoagulation

Implantation= Aspirin 81 mg + Warfarin (INR 2-3)

45 day TEE= If no leak, Aspirin 325 mg + Plavix 75 mg
Leak Present= ASA 81 mg + Warfarin

6 months post implant= ASA 325 mg daily indefinitely

How long to hold ACs before surgeries?

Always evaluate the need to hold anticoagulation vs the risk of bleeding!

NOACs should be held 2-3 days before the procedure.

Warfarin- very variable based off the patient.

Bridging for Atrial Fibrillation

High risk patients should be bridged
- CHADsVASc score of 5 or greater
- thromboembolic event within the last three months
- patients with known thrombus
- atrial fibrillation with any mechanical valve

If restarting a NOAC, then restart when okay from a surgical perspective.

Warfarin- no longer a need for bridging if low risk atrial fibrillation.

Reversal Agents

Coumadin

Vitamin K 5-10 mg IV + Promthrombinex VF 50 IU/kg IV + FFP

4 Factor Prothrombin complex concentrate (PCC)

Reversal Agents- NOACs

Idaruvizumab (Praxabind): 2.5 mg in 50 ml NS x 2 less than 15 minutes apartment

REVERSE-AD: shows reversal of Pradaxa in 88-98% of patients who had elevated aPTT at baseline.

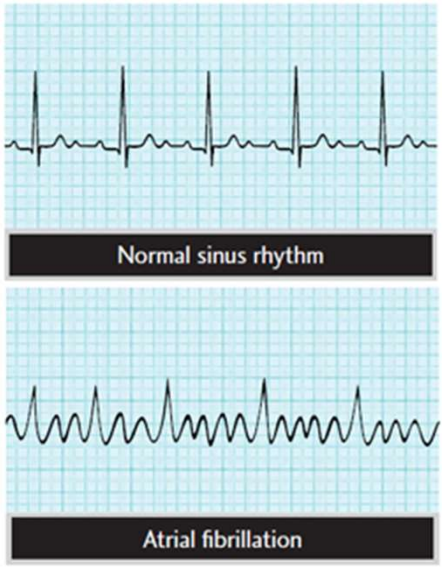
Andexxa: Dose is variable based off of dose amount and time since last dose.

ANNEXA Phase 3 studies showed a median 97% decrease in Factor Xa for patients taking rivoraxaban and 92% for apixiban

Rate Control vs Rhythm Control

Is there any benefit to maintaining rhythm over rate control?

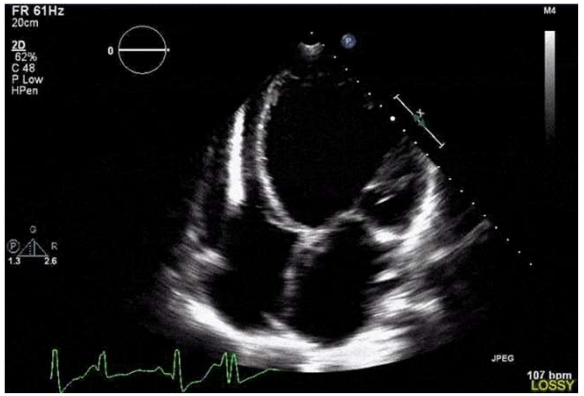
AFFIRM Trial- 2002



First major trial to ask if there was any stroke or survival benefit in rate vs rhythm control. Could use B blocker, non-dhp CCB, or digoxin. All patients were anticoagulated w/ warfarin but could be stopped if the patient was in NSR for 4 or more weeks.

No survival or stroke benefit. The rhythm control trended towards a non-significant increase in mortality.

What about in Heart Failure?



“Rate Control vs Rhythm Control for A-Fib and HF”

Looked at 1376 patients with with EF’s below 35% and randomly assigned them to rate vs rhythm control.

No increase in rate of death from cardiovascular, death from other causes, worsening of heart failure, or stroke.

Rhythm control actually required more frequent hospitalizations due cardioversions and titration of antiarrhythmics.

Rhythm Control

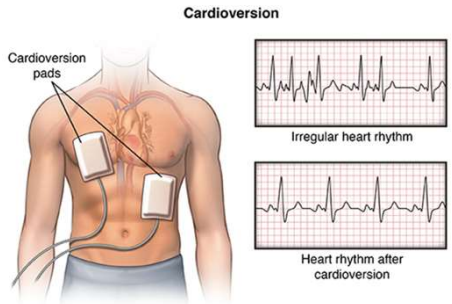
Benefits of Rhythm Control

- Symptom reduction
  - Increased exercise capacity and quality of life
  - Patients <65 tend be more symptomatic and don't tolerate the decreased atrial output.
- Prevent tachy induced cardiomyopathy

Rhythm control does NOT allow a patient to come off of anticoagulation or rate or rhythm control medication.

- AFFIRM trial showed that there was no difference in the rate of stroke in rate vs rhythm control patients.

Rhythm Control- How to convert



Electrically/Cardioversion
Pros: Usually successful. Can be done quickly.
Cons: It hurts if no anesthesia. If not anticoagulated, can cause a stroke- needs to be anticoagulated at least 3 weeks beforehand.

Chemically (Ibutilide)
Pros: Doesn't require anesthesia
Cons: Variable success rate. Stroke

Rhythm Control - Post Cardioversion

Still have a high risk of stroke post cardioversion due to atrial stunning

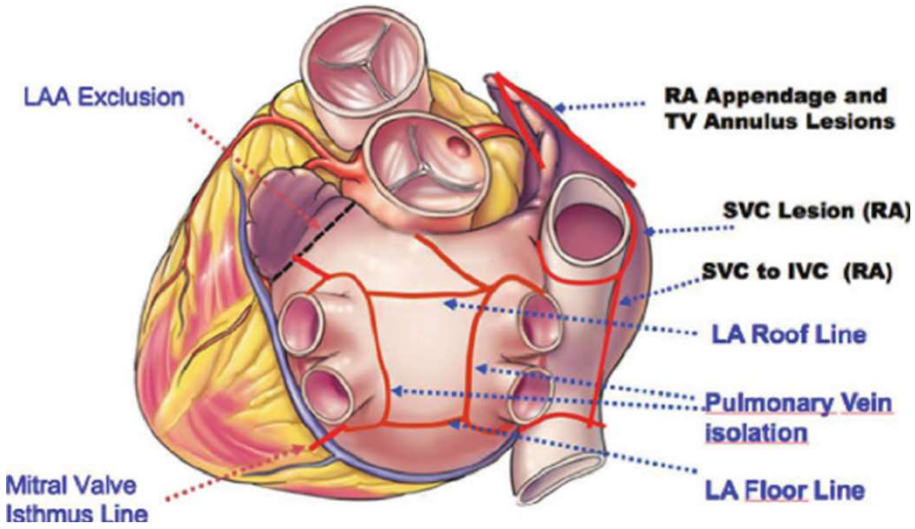
All patients needs to be anticoagulated regardless of theirs CHADS score for a minimum of 4 weeks.

Rhythm Control- Surgical

Cox Maze Procedure

Pulmonary Vein Isolation

Cox MAZE Procedure



Based off of the Wavelet and Rotor Theory

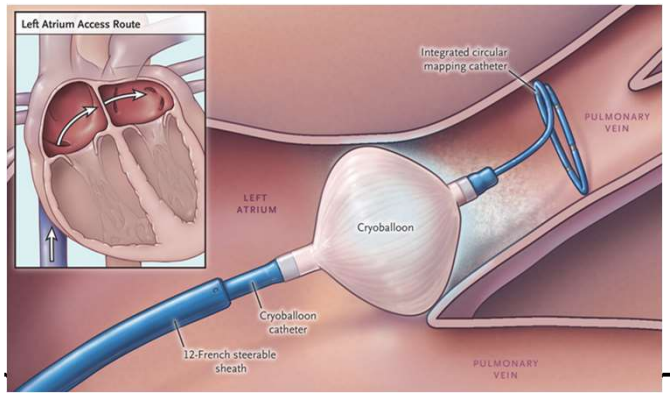
- By creating scar tissue in a specific pattern, the electrical signal can only travel one way and this scar tissue breaks up the wavelets.

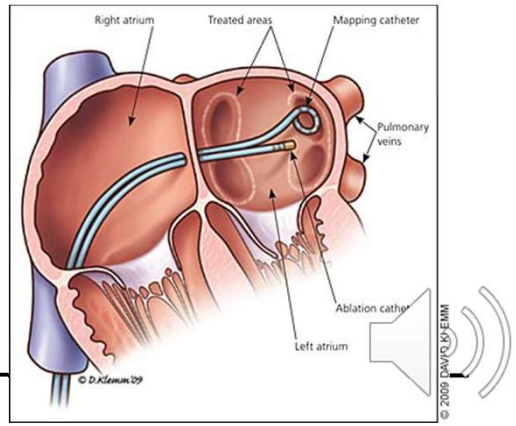
GW Cardiac Surgery is currently practicing the Cox IV Maze procedure.

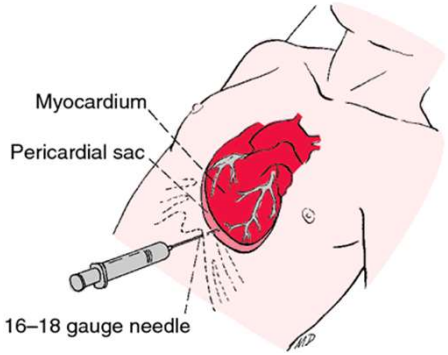
Pulmonary Vein Isolation

EP lab procedure where the pulmonary veins are electrically isolated from the atrium.

2 Techniques: Radiofrequency and Cryoablation

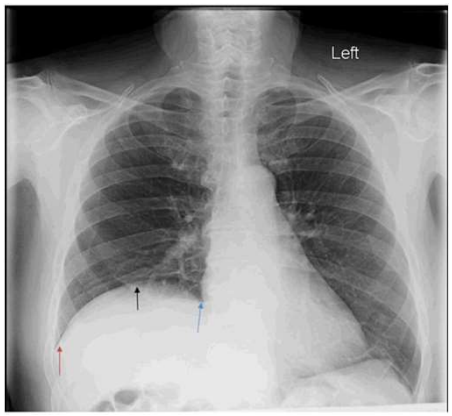






Pulmonary Vein Isolation

Potential Complications: Bleeding, pleuritic chest pain, perforation causing tamponade, phrenic nerve injury, atrial-esophageal fistula.



Success rate is based off of duration of atrial fibrillation and concurrent risk factors for atrial fibrillation.

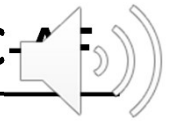
Patients will likely continue to require antiarrhythmic for a minimum of 90 days and anticoagulant medications for life.

Pulmonary Vein Isolation and Heart Failure

CASTLE AF

Patients with heart failure and paroxysmal or persistent atrial fibrillation who underwent a PVI showed reduced all caused mortality and reduced admissions for worsening heart failure when compared to medical management.

Similar conclusions were found by PABA CHF, ARC-AF



Rate Control

Common Medications

- Beta blockers
- Non-DHP Calcium Channel Blocker: Diltiazem or Verapamil
- Amiodarone (Rhythm control w/ beta blocker)
- Digoxin

Classification of Antiarrhythmic Meds

Class I: Interfere with the sodium channel

Class II: Anti-sympathetic nervous agents (Beta Blockers)

Class III: Affect potassium efflux

Class IV: Affect the calcium channel and the AV Node

Class V: Other

Class I

Class Ia: Procainamide, Disopyramide

- **Procainamide is indicated in WPW**
- **Disopyramide is usually used in patients with Hypertrophic Cardiomyopathy**

Class Ib: Lidocaine (IV), Mexiletine (PO)

- **Used to treat VT**

Class Ic: Flecainide, Propafenone

- **Prevents paroxysmal atrial fibrillation**

Class II- Beta Blockers

Carvedilol

Metoprolol

Atenolol

Bisoprolol

Nebivilol

Class III

Amiodarone

- most effective of all the antiarrhythmics. Indicated in almost all abnormal arrhythmias.

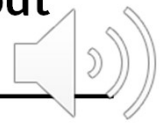
- also the most toxic. Need to closely monitor lungs, thyroid, eyes, and liver.

Ibutilide

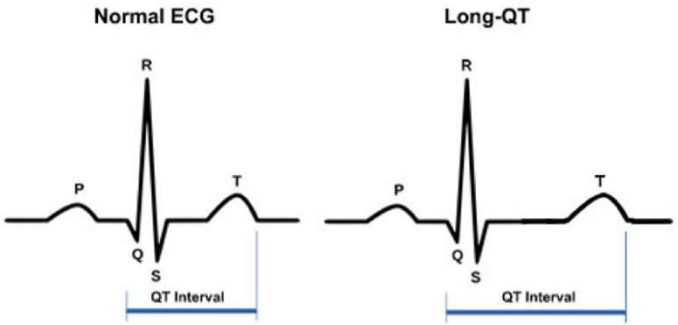
- only used for cardioversion

Dronedarone (Multaq)

- “Amiodarone lite”. Similar in structure to amiodarone but also less effective



Class III



Dofetilide (Tikosyn)
- great drug for paroxysmal atrial fibrillation. Needs to be loaded in the hospital due to prolongation of QT.

Sotalol (also has some class II activity)
- can also be used for VT. Need to be careful with patients that have renal impairment.
- recommendation is to have the patient admitted and monitored for QT prolongation

Class IV- NDHP CCB

Diltiazem

Verapamil

Class V- Others

Digioxin

- no mortality benefit. Has only been shown to reduce readmissions.

- needs to be very closely monitored in patients with renal impairment.

- Can be used to achieve rate control in patients with cardiogenenic shock

Magnesium Sulfate

- important part of the cardiac cycle and hypomagnesia is a common cause of arrhythmias.

Considerations w/ Antiarrhythmics

CAST I and II Trials: showed that using Class 1C medications in patients post MI reduced ectopy but significantly increased cardiac deaths due to arrhythmias, cardiogenic shock, and all cause cardiac arrest death.

From these trials, the only medications that are allowed post-MI or in systolic heart failure are class II medications, Tikosyn, amiodarone, and digoxin.

Pulmonary Vein Isolation First?

- EARLY-AF Trial looked at cryoablation vs anti-arrhythmic therapy for first line treatment in symptomatic atrial fibrillation
  - Ablation had less occurrence of atrial arrhythmia on long term monitors: 42.9% vs 67.8%
  - Ablation patients had fewer serious complications: 3.2% vs 4%

Special Populations

- Anticoagulation with DAPT
- Atrial Fibrillation in the ICU
- WPW and Atrial Fibrillation
- Atrial Fibrillation and Hypertrophic Cardiomyopathy (HCM)

Triple Agent Therapy

Triple Agent Therapy: OAC + ASA + P2Y12 Inhibitor

This will be seen in the patient that had a recent stent placed and has atrial fibrillation

ISAR-TRIPLE: No significant increase in in-stent thrombosis when dropping plavix at 6 weeks vs 6 months.

AUGUSTUS: no increase in coronary events or bleeding when using a P2Y12 (ie clopidogrel) and Apixiban compared to triple therapy

2019 guidelines recommend stopping aspirin at 6 weeks.

New Onset Atrial Fibrillation in ICU

New onset post op atrial fibrillation is managed differently

Very common.

Up to 65% of post cardiac surgery patients and 20% of medical ICU patients.

Usually transient.

Less than 20% of patients develop NOAF in the ICU leave w/ a-fib. Almost all convert within 6-8 weeks.

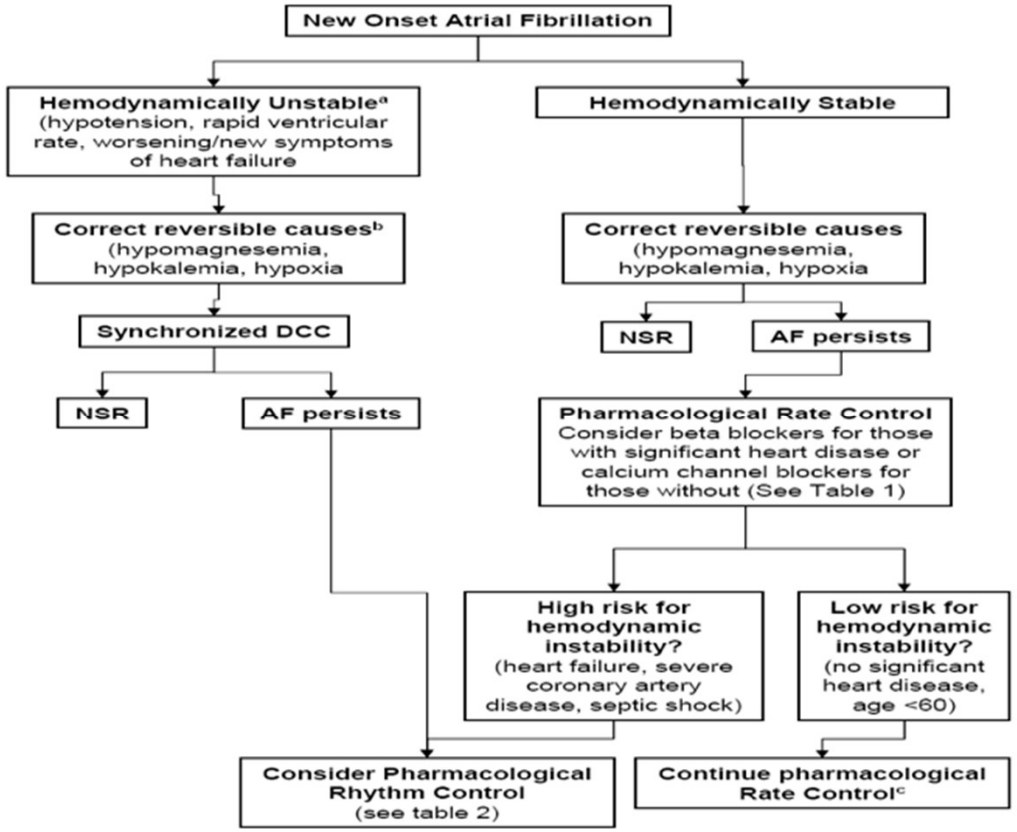
NOAF nearly doubled the rate of mortality in surgical, septic, and trauma ICU patients.

New Onset Atrial Fibrillation in ICU

If the patient is not hemodynamically unstable from the a-fib, then the goal should be rate control using beta blockers.

Amiodarone may be no better than placebo in converting patients to NSR. Conversion rate was 67% w/ amio and mag IV conversation rate was 72.2%

ADDRESS UNDERLYING ISSUES! Electrolytes, fluid overload, ischemic, hypoxemia, etc.


New Onset Atrial Fibrillation
Hemodynamically Unstable[a] (hypotension, rapid ventricular rate, worsening/new symptoms of heart failure
Hemodynamically Stable
Correct reversible causes[b] (hypomagnesemia, hypokalemia, hypoxia
Correct reversible causes (hypomagnesemia, hypokalemia, hypoxia
Synchronized DCC
NSR
AF persists
NSR
AF persists
Pharmacological Rate Control Consider beta blockers for those with significant heart disase or calcium channel blockers for those without (See Table 1)
High risk for hemodynamic instability? (heart failure, severe coronary artery disease, septic shock)
Low risk for hemodynamic instability? (no significant heart disease, age <60)
Consider Pharmacological Rhythm Control (see table 2)
Continue pharmacological Rate Control[c]

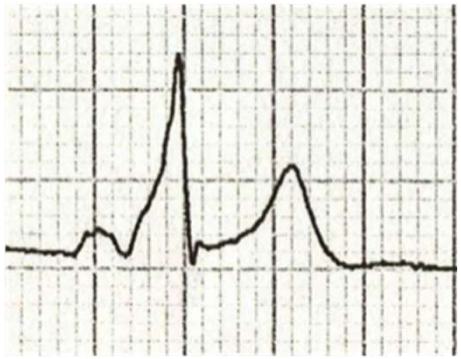
Post Op A-Fib

Pre Op beta blockers reduce the incidence of atrial fibrillation by 72%.

For cardiac surgery pts: post op pacing w/ beta blocker further reduces the incidence of a-fib.

Trying to attempt to achieve rhythm control in new onset AF in the ICU leads to increased costs and potentially more days in the ICU. No difference in readmission rates, stroke, bleeding, or mortality.

Atrial Fibrillation w/ WPW

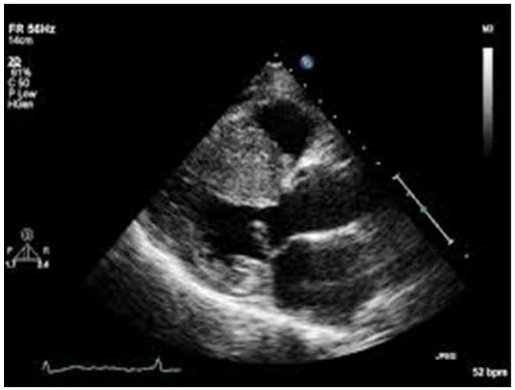


Patient w/ pre-excited pathways that are extremely fast and atrial fibrillation can rapidly devolve into V-Fib requiring immediate cardioversion.

Drugs to avoid: AV nodal blocking agents.
Electrical Cardioversion is the safest for people w/ WPW and SVTs. Can also use procainamide.

EP study w/ ablation is the definitive treatment and is a class I recommendation for patients w/ WPW

Atrial Fibrillation and HCM



Extremely Common- 20% prevelance of patients with HCM

Patients w/ hypertrophic cardiomyopathy rely very heavily on their atrial kick and are extremely symptomatic.

Very high risk of stroke

Atrial Fibrillation and COVID

- Patient's with pre-existing atrial fibrillation/flutter had a higher risk of death or ICU mortality
- Patients who developed intra hospital atrial fibrillation/flutter had significantly increased risk of death or ICU mortality

Post Test Questions- Question 1

65 y/o gentleman with a past medical history of HTN, DM II, and a MI 3 years presents to your office with complaints of palpitations for the past 12 hours. You do an EKG and find that he is in atrial fibrillation. He refuses to undergo a transesophageal echocardiogram before the test. What is the minimum amount of time he should be on anticoagulation before your cardiovert him?

How long to anticogulate?

A) 1 week

B) 2 weeks

C) 3 weeks

D) 4 weeks

Post Test Question 2

The same gentleman get successfully cardioverted! You know decide that he will require medication therapy to stay in normal sinus rhythm. What medication is not allowed in this patient.

Which medication should you avoid?

A) Metoprolol Succinate

B) Digoxin

C) Tikosyn

D) Flecanide

Post Test Question 3

You are taking care of 75 y/o female with permanent atrial fibrillation, diabetes, HTN, CAD s/p stenting 10 years ago, and ESRD on MWF dialysis. She has no real complaints but you draw her INR today and you find that it is 1.7. When you review the chart, you find that is frequently sub-theraputic over the last 6 months. You discuss this with her and she says that she has a new found love of leafy vegetables. What anticoagulant would be reasonable to change her to?

What anticoagulant?

A) Dabigitran

B) Apixaban

C) Rivoraxaban

D) Endoxaban

THANK YOU!