

## Atrial Fibrillation

Current Management for the Family Physician  
 Clare Hawkins MD MSC FAAFP  
 NDAFP Big Sky CME  
 Tuesday January 18, 2022 6-6:45p

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## Recommendations

1. Rate Control over Rhythm Control
  - (Strong rec/ high evidence)
2. Target Lenient rate control <110 bpm
  - (Weak rec/ low evidence)
3. Discuss Risk of Stroke & Bleeding in patients with A Fib using CHADS2 and HASBLED scores
  - (Weak rec / low evidence)
4. Prescribe chronic anticoagulation unless they are at low risk of stroke (CHADS2 <2) or have specific contraindications
  - (Strong rec / high evidence)

AAFP 2017 guidelines  
<https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/atrial-fibrillation.html>

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## Objectives

1. Utilize current clinical practice guidelines for the management of AF, and the CHADS2 index to prescribe appropriate medications
2. Review the coagulation cascade and compare targets of medications that affect the coagulation pathway with specific applications to current recommendations of medications for patients with atrial fibrillation
3. Prepare treatment plans for patients (especially the elderly) who present with atrial fibrillation
4. Educate patients on lifestyle modifications they can make to ensure heart health and prevent complications from AF, including stroke or heart failure

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## Practice Gaps

- Family physicians have a knowledge and performance gap related to the selection of appropriate cardiac imaging modality for specific cardiovascular problems
- Physicians are often inconsistent with regard to therapeutic decision making for patients with AF
- Physicians frequently exhibit poor communication between caregivers for elderly patients with AF

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## Practice Gaps

- Physicians are inconsistent with their long-term management of AF patients
- Physician adherence to oral anticoagulation therapy initiation is low among AF patients
- Awareness & Implementation of AAFP 2017 guidelines for Management of Newly Detected Atrial Fibrillation

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## Terminology

- Supraventricular arrhythmias
  - Sinus Tachycardia (the most common)
    - Secondary rhythm (220-age) p before QRS
    - Onset and termination gradual
    - A response to a physiological event
  - Atrial flutter (transitional) 280-330 bpm
  - Atrial fibrillation (AF) irreg. irreg. 60-220 bpm

Atrial Fibrillation ACC 2006 Guideline Circulation. August 15, 2006 2006;114(7):700-752

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## Atrial Fibrillation: Definitions

Term	Definition
Paroxysmal AF	AF which terminates spontaneously or with intervention within 7 days
Persistent AF	Continuous AF sustained > 7d
Long-standing persistent AF	Continuous AF > 12 m
Permanent AF	Once patient & physician decide not to attempt to restore NSR
Nonvalvular AF	In the absence of rheumatic Mitral Stenosis, mechanical or bioprosthetic valve, or valve repair

Adapted from table 3 ACC 2014 A Fib Guideline JACC vol 64, No. 21 2014

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## “Lone” Atrial Fibrillation

- Individuals under age 60
- No clinical or echocardiographic evidence of disease, including HTN
- Occurs in:
  - 30-45% of those with paroxysmal AF
  - 20-25% of those with persistent AF
  - A responsible underlying condition may appear over time

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## A fib Epidemiology

- Projected increase from 5.2 million in 2010 to 12.1 million cases in 2030
- Most common arrhythmia in clinical practice
- Most common type of serious arrhythmia
- 1/3 of hospitalizations for cardiac rhythm disturbances
- 2.3 million people in US

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## Stroke Epidemiology

- Risk of stroke from A fib increases as people age
- A fib gives a five-fold risk increase in mortality
- Incorporated into CHA<sub>2</sub>DS<sub>2</sub>VASc score

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## Outcomes

- Increased risk of stroke
- Increased severity of heart failure
- Increased mortality, especially among women
- Discomfort/ Palpitations / Syncope

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## Pathophysiology

- Multifactorial Etiology
- Multiple diseases contribute to final common pathway of altered electrical conduction and lack of sequential contraction of atrium to ventricle
- Uncoordinated electrical activation of the atria and an irregular, often rapid, ventricular response
- Fibrillating Atrium vulnerable to clot formation which can propagate to the brain causing stroke
  - reduces effectiveness of cardiac contraction increasing HF

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## Atrial Fibrillation Pathophysiology

Extra Cardiac	Structural	Electrical
Hypertension	Dilation	↓ Conduction
Obesity	Inflammation	↓ Action Potential Refractoriness
Alcohol	Fibrosis	↑ Heterogeneity
OSA	Hypertrophy	↑ Automaticity
Drugs	Ischemia	↑ Heterogeneity
		Altered Ca++ handling

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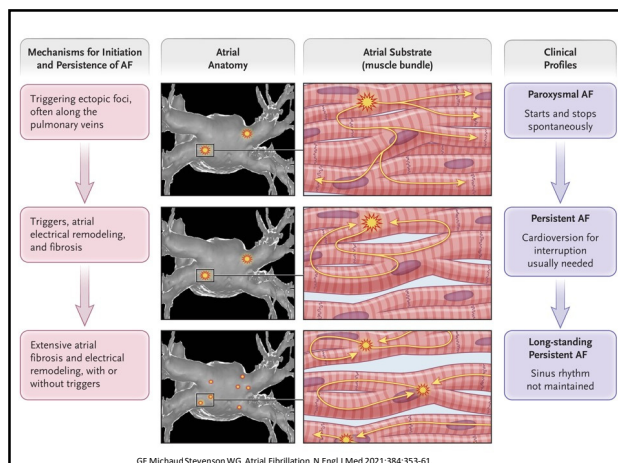
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Non Cardiac	Cardiac
Thyroid	CHF
Sleep Apnea	Dilated Cardiomyopathy
Pulmonary Embolism	Ventricular Hypertrophy
COPD & Cor Pulmonale	CAD (ischemia)
Collagen Vascular	Atrial Septal Defect
Pneumonia	Valvular disease
Illicit Drugs	Tricuspid Valve (Ebstein)
Drugs which increase QT	Post cardiac surgery
B agonist inhalers	Post ablation therapy
Lithium	Post cardiac catheterization
Antiarrhythmics	Epicardial injury
Diet Pills-Stimulants	Myocardial diseases (infectious, toxicity)

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## Diagnosis

- Physical examination, electrocardiography, chest radiography, two-D echocardiography, CBC, electrolytes, liver and kidney function tests, TSH
- suspected atrial fibrillation should be confirmed with 12-lead electrocardiography
- Screening EKG is not recommended
- Absent P, chaotic atrial activity, irregular R-R intervals, narrow QRS
- Optional: Event recorder, polysomnography, PFT
- Trans Thoracic Echo (TTE)

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## Recommendation #1

- Rate-control strategies are superior to rhythm-control strategies in reducing cardiovascular hospitalizations (GRADE....)
- Antiarrhythmic medications can be associated with significant risks and side effects including proarrhythmia
- Reduced cardiovascular hospitalizations with rate control & harms associated with antiarrhythmic medications, rate-control should be initiated for most patients with AF

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## Rate Control

- Outpatient management appropriate unless ACS or severe volume overload (ACC 2019)
- First Line
  - Beta blockers (e.g., metoprolol, carvedilol)
  - Non-dihydropyridine calcium channel blockers (e.g., diltiazem, verapamil)
- Second Line
  - Digoxin (0.125 daily dose in elderly, EOD in those with renal failure)

AAFP 2017 Guideline: <https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/atrial-fibrillation.html>

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## So, when do you try to pursue rhythm control?

- Rhythm control is an option for treatment of AF for patients whose symptoms are not managed by rate control
  - (weak rec / Low- quality evidence)
- Options: amiodarone, dronedarone, propafenone, and sotalol

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## Recommendation # 2 Lenient Rate Control

- The AAFP recommends lenient rate control (<110 beats per minute resting) over strict rate control (<80 beats per minute resting) for patients with atrial fibrillation
  - (weak rec / low- quality evidence).
- Despite no evidence showing superiority of strict control (<80 beats per minute resting), it is preferentially recommended by the AHA/ACC/HRS guideline

AAFP 2017 Guideline: <https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/atrial-fibrillation.html>

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## Rate Control Merits

- Rate control
  - improves diastolic filling
  - Improves coronary perfusion
  - decreases myocardial energy demand
  - prevents tachycardia-mediated cardiomyopathy
  - The goal is to achieve a ventricular response of less than 80 beats per minute at rest and less than 110 beats per minute during exercise ("Lenient")

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## Rate Control

- Beta Blocker (ie metoprolol)
- Non Dihydropyridine Ca Channel Blocker
  - Diltiazem, Verapamil
- Digoxin not optimal but can help with HF
- Pacemaker
  - Ablate AV node and pace the ventricle
  - Alternate pacing alternatives
  - Not responsive to exercise HR demand increase

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### Patient oriented outcomes versus theoretical outcomes

- Of course NSR will have a better ejection fraction
- NSR prevents atrial remodelling and decreases the chance of being able to stay in NSR
  - But at what cost?
- It is difficult to keep in NSR
- Medications to “convert” are have many side effects

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### When would you try to achieve NSR

- Reversible causes of A fib
- New Onset of A Fib
- Even persistent A fib if less than a year
- Symptomatic A fib in spite of rate control

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### Cardioversion

- Electrical cardioversion usually successful in the short term
- Anticoagulation important prior to cardioversion
- If TEE shows no thrombus in the left atrium you do not need precardioversion anticoagulation

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### Cardioversion

- Electrical cardioversion
  - Direct- current electric shock in synchrony with the QRS complex to avoid triggering ventricular brillation
  - 200 to 300 joules, may repeat
- Pharmacologic cardioversion
  - intravenous ibutilide (Corvert)
  - Flecainide (Tambocor)
  - dofetilide (Tikosyn)
  - Propafenone (Rythmol)
  - Amiodarone. (Cordarone, Nexterone, Pacerone)

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### Cardiac (Electrical) Ablation

- Catheter-based procedure used to isolate and possibly destroy abnormal foci
- Sites near the pulmonary vein ostia in L atrium
- Many patients require repeat ablation and patient may revert to a fib over several years
- Many patients are required to remain on anticoagulation because of future risk of A. fib.
- Ablation therapy may be superior to antiarrhythmics in selected patients
  - Symptomatic PAF without structural heart disease
  - Intolerance for antiarrhythmics
  - Inadequate pharmacologic rhythm control

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### Evolution of Electrical Ablation

- 2014 ACC guideline gave IIa recommendation as reasonable initial rhythm-control strategy<sup>1</sup>
- Radiofrequency energy with mixed results
- Cautious recommended for select young patients with symptomatic AF and understand benefits/risk<sup>2,3</sup>
- CABANA trial showed electrical ablation not superior to medication in 2200 patients<sup>4</sup>

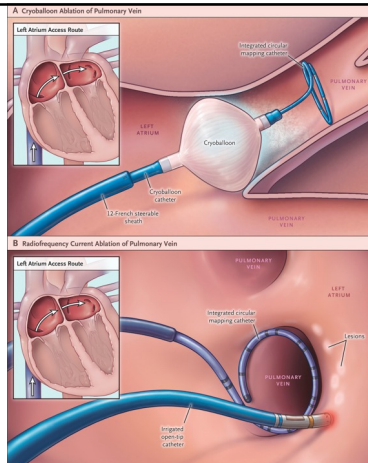
<sup>1</sup> 2014 ACC Atrial Fibrillation Guideline Circulation. 2014;130:e199-e267  
<sup>2</sup> Hakalahti A et al. Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. Europace 2015;17:370-8  
<sup>3</sup> 2019 ACC update of 2014 Atrial Fibrillation Guideline Circulation. 2019;140:e125-e151  
<sup>4</sup> Catheter ablation vs. antiarrhythmic drug therapy for atrial fibrillation: the results of the Cabana Multicenter International Randomized Clinical Trial. [abstract B-LBCT01-05] Heart Rhythm. 2018; 15:940-141

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## Balloon Cryoablation

- Subzero temperature to pulmonary-vein antra
- Radiofrequency catheter ablation with heat energy
  - Point-by-point connected lesions
  - Directed via 3-D navigational system

Ruck HZ et al. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *N Engl J Med* 2016; 374:2235-2245



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## Balloon Cryotherapy Ablation

- Proposed initial intervention before pharmacological Transatrial balloon over wire, 2 hour, 1 hour in atrium for Pulm Vein isolation then cryoablation
  - Risks: atrial-esophageal fistula, PV stenosis, phrenic nerve injury, TIA, stroke, AMI and bleed
- STOP AF (203 patients)<sup>1</sup> adv events = at 14%
- EARLY-AF (303 patients)<sup>2</sup> adv events = at 4%
  - RCT for catheter ablation with cryotherapy balloon
  - Lower recurrence rates and greater quality of life
- NEJM review 2021<sup>3</sup> Question remains as to net-safety in real life practice

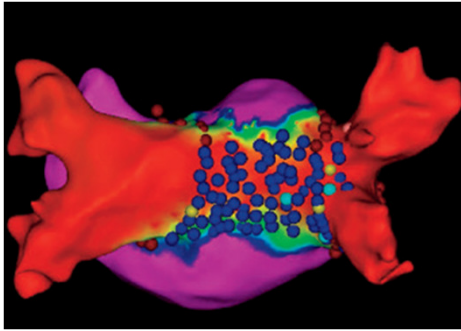
<sup>1</sup> STOP AF *N Engl J Med* 2020;384:316-24

<sup>2</sup> Early AF *N Engl J Med* 2020; 384:305-15

<sup>3</sup> Early Ablation for Paroxysmal Atrial Fibrillation – Safety First *N Engl J Med* 384:4 1/28/2021

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## Pulmonary Veins and LV Ablation



[Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation](#)  
J.G. Andrade and Others *N Engl J Med* 2021; 384:305-315

GF Michaud-Stevenson WG. Atrial Fibrillation. *N Engl J Med* 2021;384:353-61.

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## Eliminate the Atrial Appendage?

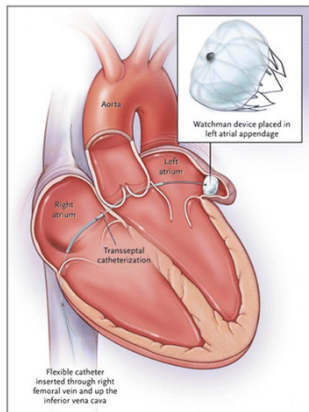


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## Fuse Procedure

- Ablation of atrial appendage
- At the time of open heart surgery
- Or catheter based device ablation
- Only for the exceptional patient
- Must continue anticoagulation



Maisel W.H. Left Atrial Appendage Occlusion — Closure or Just the Beginning? *NEJM* 360:25 *nejm.org* June 18, 2009  
Image used with permission

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## Communicating Risk Benefit Shared Decision Making



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## Shared Decision Making

- Discussion with the patient is essential to determine values and preferences before prescribing a particular anticoagulation strategy
- Explain risks, testing burden, medication adherence, and quantify stroke and bleeding risk
  - Seems overwhelming !

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## Shared Decision Making



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## Patient Preferences Doctor Preferences

- Rhythm control harder to achieve and may require more medication with an increased likelihood of side effects.
- If they are symptomatic you have to advocate for intervention
- Otherwise you need to find a way to explain quantitative risk
  - Medical literacy and numeracy show that this is difficult
  - Can't we just be paternalistic? Can we recommend...strongly?

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## Recommendation #3

- The AAFP recommends that clinicians discuss the risk of stroke and bleeding with all patients considering anticoagulation (good practice point)
- Clinicians should consider using the continuous CHADS<sub>2</sub> or continuous CHA<sub>2</sub>DS<sub>2</sub>-VASc for prediction for risk of stroke
  - (weak recommendation, low-quality evidence) and HAS-BLED for prediction of risk for bleeding (weak recommendation, low-quality evidence) in patients with atrial fibrillation.

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### CHADS<sub>2</sub>

	Risk Factor	Score
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension	1
<b>A</b>	Age 75+	1
<b>D</b>	Diabetes mellitus	1
<b>S</b>	Prior Stroke or TIA	2
Total Score for a maximum of		6

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### CHA<sub>2</sub>DS<sub>2</sub> VASc

	Risk Factor	Score
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension	1
<b>A</b>	Age 75+	2
<b>D</b>	Diabetes mellitus	1
<b>S</b>	Prior Stroke or TIA	2
<b>V</b>	Vascular disease (MI, PVD or Aortic atherosclerosis)	1
<b>A</b>	Age 65-74	1
<b>S</b>	Female	1
Total Score for a maximum of		9

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Cha <sub>2</sub> ds <sub>2</sub> VASc	Adj. Stroke Rate / yr	Chads <sub>2</sub>	Adj. Stroke Rate / yr
1	1.3	0	1.9
2	2.2	1	2.8
3	3.2	2	4
4	4	3	5.9
5	5	4	8.5
6	6	5	12.5
7	9.6	6	18.2
8	6.7		
9	15.2		

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HAS-BLED		
	Condition	
H	Hypertension: (uncontrolled, >160 systolic)	1
A	Abnormal Renal: Dialysis, transplant, Cr >2.26	1
S	Stroke: Prior history of stroke	1
B	Bleeding: Prior Major Bleeding or predisposition to bleed	1
L	Labile INR (Unstable or High) <60% time therapeutic	1
E	Elderly: Age > 65	1
D	Prior Alcohol or Drug Usage (> 8 drinks/week) Medications predisposing to bleeding (Antiplatelet or NSAID)	1

Score of >3 "high risk" 3.74% / yr, 4=8.7, 5=12.5,

Lip, Gregory Y.H. Implications of the CHA<sub>2</sub>DS-VASc and HAS-BLED Scores for Thromboprophylaxis in Atrial Fibrillation. The American Journal of Medicine. 124(2): 111-4

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### Recommendation 4

- The AAFP strongly recommends that patients with atrial fibrillation receive chronic anticoagulation unless they are at low risk of stroke (CHADS<sub>2</sub> <2) or have specific contraindications (strong recommendation, high-quality evidence)
- Patients with nonvalvular atrial fibrillation who are at low risk of stroke can be treated with 81 to 325 mg of aspirin per day.
- Choice of anticoagulation therapy should be based on patient preferences and patient history
- Options include warfarin, apixaban, dabigatran, edoxaban, or rivaroxaban

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### Warfarin

- Reduce Stroke Risk, Increase Bleeding Risk ?
- How it works to inhibit Vitamin K Dependent Clotting



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### History

- 1920s cattle in N. USA & Canada, stricken with fatal bleeding disease. Mouldy silage from sweet clover implicated.
- N. Dakota scientist L.M. Roderick showed hemorrhagic factor
- 1940 Karl Link in Wisconsin identified 4-hydroxy coumarin
- 1948 Warfarin synthesized and approved as rodenticide in 1952
- 1954 Approved for Human Use
- WARF (Wisconsin Alumni Research Foundation)
- -arin from coumarin

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### Warfarin Contraindications

- Pregnancy, except in women with mechanical heart valves
- Hemorrhagic tendencies or blood dyscrasias
- Recent or planned surgery of the central nervous system or eye, or traumatic surgery resulting in large open surfaces
- Potential high levels of noncompliance in unsupervised patients
- Hypersensitivity to warfarin
- Malignant hypertension

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## Warfarin, VKA (Vitamin K Antagonist) Safe Practices

- Safe Practices
  - Algorithm
  - Frequent follow up / systems of care
  - Weekly at initiation and monthly thereafter
  - Home INR machines, (who responds)
  - Multiples of same dose (ie. 5 mg) to prevent medical errors
- Still
  - Warfarin is #1 adverse medication reactions and visits to hospital for bleeding (1-3% of patients treated )

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INR	Low Risk of Bleed	High Risk of Bleed
INR <5 No significant bleeding	Repeat INR daily, hold next dose, resume at lower dose when INR therapeutic If only .5 above could keep same dose	Repeat INR, hold warfarin, monitor INR. Consider small 1 mg po dose vitamin K
INR ≥ 5 but <9 No sig bleeding	Repeat INR daily, hold warfarin, resume at lower dose	Repeat INR q 12 h, consider Vit K 2.5 po. (1 mg iv?)
INR > 9, no bleeding	Repeat INR daily, hold warfarin. Consider oral Vit K 2.5-5 mg. Resume at lower dose when therapeutic	Repeat INR q 12, Consider Vit K 2.5-5 mg. (IV 1-2.5 mg slowly over one hour) Repeat Vit K as necessary
Serious Bleeding at any INR	Hold warfarin. IV Vit K 10 mg over one hour. Monitor INR q 6 h. Repeat Vit K if not fully corrected in 24 h. Consider FFP 10-15 ml/kg IV, Recombinant Human factor VII or prothrombin complex concentrate	
Life Threatening Bleeding	Hold warfarin. IV Vit K over 1 h. recomb factor IV, or Prothrombin complex concentrate or FFP monitor INR q 2 h	

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## Bridging

- Holding oral anticoagulation and using Heparin (UFH or LMWH) for a procedure
- Oral Anticoagulation (OAC) should not be interrupted for procedures with low bleeding risk
- Low risk of thromboembolism should not be bridged
- Of 35 m patients on OAC 15-20% will need a procedure annually.
- 44% overuse of bridging

Rechenmacher SJ and Fang JC Bridging Anticoagulation Primum Non Nocere J Am Coll Cardiol 2015;66:1392-403  
Kovacs RJ, Flaker GC, Saxonhouse SJ, et al. Practical management of anticoagulation in patients with atrial fibrillation. J Am Coll Cardiol. 2015;65(23):2340-2360.  
Droukettis JD, Spyropoulos AC, Kaatz S, et al.; BRIDGE Investigators. Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med. 2015;373(9):823-833

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## Warfarin Cost Effective?

- Medication Cost small
- Monitoring adds to cost if you include transportation, labs etc.
- Cost of Home Monitoring equipment
- Cost of Side Effects
- Impact on Quality of Life (diet)

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## Coumadin Diet?

- Be consistent in the amount of vitamin K you eat from day to day
- Most dark green leafy vegetables are high in vitamin K. But so are some other foods and oils
- Avoid herbal teas containing coumarin, such as chamomile, sweet clover or sweet woodruff teas
- Avoid fish oil, walnut oil, flaxseed oil, garlic oil, ginger, onion extract pills, vitamin C or E (in amounts greater than the RDA), coenzyme Q-10, glucosamine, or alfalfa

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## Direct Oral Anticoagulants, DOAC

- (Formerly NOAC Novel or Non Vitamin K Anticoagulants)
- 2019 ACC guideline recommends DOAC over VKA
- Direct thrombin inhibitors
  - Dabigatran etexilate (Pradaxa)
- Direct factor Xa inhibitors
  - Apixaban (Edoxaban)
  - Rivaroxaban (Xarelto)
  - Edoxaban (Sayvasa)

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### Dabigatran Dosing Good Rx \$460.00 / mo

Reduction in Risk of Stroke		
Renal Function	Recommended Dose	Concomitant Use of P-gp Inhibitors Dronedronone Ketonconazole
Normal or Mild	150 bid	150 bid
Moderate < 50 gfr	150 bid	75 bid
Severe < 30 gfr	75 bid	Avoid
V. Severe < 15 gfr	Avoid	Avoid

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### Apixaban (Eliquis) Dosing Good Rx \$508.00 / mo

- 5 mg daily 2.5 mg for patients with any two of the following:
  - age 80 years or older
  - body weight less than 133 lb (60 kg)
  - serum creatinine level of 1.5 mg per dL

Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. N Engl J Med. 2011;364(9):806-817  
<http://www.aafp.org/afp/2014/0415/p672.html> accessed July 12, 2017

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### Rivaroxaban (Xarelto) Dosing Good Rx \$ 499 / mo

- **Nonvalvular Atrial Fibrillation:**
  - CrCl >50 mL/min: 20 mg po daily with evening meal
  - CrCl 15 - 50 mL/min: 15 mg po daily with evening meal
- Treatment of DVT, PE, and Reduction in the Risk of Recurrence of DVT and of PE
  - 15 mg po daily with food for the first 21 days
  - 20 mg po daily with food thereafter
- Long-term reduction in the risk of recurrence of DVT and of PE & Prophylaxis of DVT Following Hip or Knee Replacement Surgery
  - 10 mg po daily with or without food

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### Edoxaban (Savaysa) Dosing Goodrx.com \$ 400/ mo

- Cr. Cl > 50 = 60 mg po daily
- Cr. Cl < 50 = 30 mg po daily

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### Reversing DOAC effect If major bleeding

- Significantly reduced activity of DOAC after 12 hours, so waiting is the primary strategy
- Surprisingly this does not happen often, and much less than Warfarin therapy
- Supportive care as appropriate for location of bleeding
- Andexanet Alpha (ANDEXXA) approved by FDA and available in large centers to treat severe bleeding (ie. Intracranial)

Siegal DM, Currutte JT, Connolly SJ, et al. Andexanet alfa for the reversal of factor Xa inhibitor activity. N Engl J Med. 2015;373(25):2413-2424

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### What to do if A fib in setting of PCI (Coronary Stent)

- What about patients on Thienopyridine
  - Clopidogrel, Prasugrel, Ticagralor?
    - Increased bleeding risk
- Not equivalent stroke prevention to Warfarin or DOAC?
- Adding Dual Antiplatelet (ASA + Thienopyridine) to DOAC or warfarin triples the risk of bleeding

Halperin JL, et al ACA AHA Focused update on Duration of Dual Antiplatelet Therapy. JACC 68(10) 2016 1082-115

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### Triple Therapy: A fib + PCI

- Approximately 5% of patients undergoing Percutaneous Coronary Intervention, (PCI) have atrial fibrillation and require long-term oral anticoagulant therapy
  - Balance risk of bleeding with
  - Risk of stroke or stent thrombosis
- ACC 2019 update for A fib recommends
  - Clopidogrel over prasugrel if triple therapy indicated
  - Clopidogrel and low-dose rivaroxaban 15 mg is a reasonable alternative

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### Summary

- Prevention:
  - Exercise, diet, weight reduction, smoking cessation, avoid unnecessary medications, avoid excess alcohol
- Evaluation:
  - Reversible causes, underlying etiology
- Intervention:
  - NSR with Ablation or pharmacotherapy
  - Permissive rate control and anticoagulation for stroke prevention

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