



# Anticoagulants in Atrial Fibrillation

## Starting and Stopping Them Safely


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Atrial Fibrillation Anticoagulation

## Overview

- Learning objectives
- Introduction
- Basic concepts
- Treatment strategy & options
- Summary



Atrial Fibrillation Anticoagulation

## Learning objectives

1. List the major considerations to be addressed in the management of atrial fibrillation.
2. Determine which patients with atrial fibrillation are appropriate candidates for anticoagulation.
3. Compare and contrast the various oral anticoagulants currently available for stroke prevention in atrial fibrillation.
4. Describe the adjustments in dosage or choice of oral anticoagulant that may be necessary due to changes in patients' renal or hepatic function.

Atrial Fibrillation Anticoagulation

## Learning objectives (cont.)

5. Explain the safest way to stop and restart the various oral anticoagulants for procedures that carry considerable bleeding risk.



## Atrial Fibrillation Anticoagulation

## Introduction

### Atrial fibrillation (AF) *prevalence*

- 5.2 million persons in the United States afflicted with AF (2010 data)
- *Projected* AF prevalence in the United States in 2030: 12.1 million
- Increases with age
  - 0.1% of adults younger than 55 years
  - > 9% of adults 80 years or older

## Atrial Fibrillation Anticoagulation

## Introduction (cont.)

### Atrial fibrillation (AF) *incidence*

- Increases with age:
  - < 0.1 % per year in people < 40 years old
  - > 1.5 % per year in women > 80 years old
  - > 2 % per year in men > 80 years old



## Atrial Fibrillation Anticoagulation

**Introduction (cont.)****Definitions of AF**

- Paroxysmal
- Persistent
- Permanent
- Nonvalvular
- Lone

## Atrial Fibrillation Anticoagulation

**Cornerstones of AF Management**

## Atrial Fibrillation Anticoagulation

### Cornerstones of AF Management

## Emerging 4<sup>th</sup> pillar in AF management:

### AF Risk Factor Modification

**Obesity**  
**Low cardiorespiratory fitness**  
**Obstructive sleep apnea**  
**Hypertension**  
**Hyperlipidemia**  
**Diabetes mellitus**  
**Coronary artery disease**

Miller JD et al. *J Am Coll Cardiol.* 2015;66:2899-2906.

## Atrial Fibrillation Anticoagulation

# Basic Concepts

- **Antithrombotic therapy**
  - **Rationale**
    - **CVA risk**
      - AF = 5 x age-matched controls
      - AF = A. flutter
      - Paroxysmal = Persistent = Permanent



## Atrial Fibrillation Anticoagulation

**Basic Concepts (cont.)**

- **Antithrombotic drugs**
  - **Interfere with thrombus formation**
  - **Include:**
    - **Antiplatelet drugs**
      - Interfere with *platelet plug* formation
    - **Anticoagulant drugs**
      - Interfere with *fibrin* formation



## Atrial Fibrillation Anticoagulation

**Basic Concepts (cont.)**

- **Thrombus composition varies with the site of thrombus formation**
  - **Thrombi that form in arteries (high flow conditions)**
    - Platelets predominate
    - Relatively little fibrin
    - “White thrombi”
  - **Thrombi that form in veins (slow flow conditions)**
    - Rich in fibrin and trapped red blood cells
    - Relatively few platelets
    - “Red thrombi”



## Strategy for Antithrombotic Selection

PATHOGENESIS	
Arterial Platelets and fibrin (PI and/or A/C)	Acute cor. syndr. PCI
Chambers / Venous	A. fib. Very low LVEF DVT
Fibrin (A/C)	Pulm. embolism
Prostheses Fibrin more than platelets  (A/C > PI)	

### Atrial Fibrillation Anticoagulation

## Treatment Strategy / Options (cont.)

- **Antithrombotic therapy (cont.)**
  - Antithrombotic strategy must be *individualized* based on risk stratification
    - For nonvalvular AF, the CHADS<sub>2</sub> scoring system and, more recently, the CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring system is a useful method for estimating stroke risk in AF patients.

## Atrial Fibrillation Anticoagulation

## Treatment Strategy / Options (cont.)

- **Antithrombotic therapy (cont.)**
  - Antithrombotic strategy must be *individualized* based on risk stratification (cont.)
  - These scoring systems, along with the HAS-BLED bleeding risk scoring system, may be used to guide antithrombotic therapy.



## Atrial Fibrillation Anticoagulation

CHADS<sub>2</sub> Risk Stratification Scheme

Risk Factors	Score
<b>C</b> Congestive heart failure	1
<b>H</b> Hypertension	1
<b>A</b> Age $\geq 75$ years	1
<b>D</b> Diabetes mellitus	1
<b>S<sub>2</sub></b> History of stroke or transient ischemic attack	2

Rockson et al. *J Am Coll Cardiol.* 2004;43:929-935.



## Atrial Fibrillation Anticoagulation

CHADS<sub>2</sub> Risk Stratification Scheme (cont.)

Score	Recommended therapy
0	Aspirin (81 to 325 mg daily)
1	Aspirin (81 to 325 mg daily) or Warfarin (INR 2.0 – 3.0)
2 - 6	Warfarin (INR 2.0 – 3.0)

Rockson et al. *J Am Coll Cardiol.* 2004;43:929-935.

## Atrial Fibrillation Anticoagulation

CHA<sub>2</sub>DS<sub>2</sub>-VASc Risk Stratification Scheme

Risk Factors	Score
<b>C</b> Congestive heart failure	1
<b>H</b> Hypertension	1
<b>A<sub>2</sub></b> Age ≥75 years	2
<b>D</b> Diabetes mellitus	1
<b>S<sub>2</sub></b> History of stroke or transient ischemic attack	2
<b>V</b> Vascular disease	1
<b>A</b> Age 65 - 74 years	1
<b>Sc</b> Sex category (female gender)	1

Lip et al. *Chest.* 2010;137:263-272.

## Atrial Fibrillation Anticoagulation

### CHA<sub>2</sub>DS<sub>2</sub>-VASc Risk Stratification Scheme (cont.)

Score	Recommended therapy
0	"It is reasonable to omit antithrombotic therapy."
1	**** "No antithrombotic therapy, treatment with oral anticoagulant, or aspirin may be considered."
≥ 2	"Oral anticoagulants recommended."



January et al. *J Am Coll Cardiol.* 2014;64(21):2246-2280.

## Atrial Fibrillation Anticoagulation

### CHA<sub>2</sub>DS<sub>2</sub>-VASc Score of "1"

\*\*\*\* Females with a CHA<sub>2</sub>DS<sub>2</sub>-VASc Score of "1" are probably truly low-risk for stroke (and may not require anticoagulation for nonvalvular AF), whereas males with a CHA<sub>2</sub>DS<sub>2</sub>-VASc Score of "1" are probably at higher risk for stroke (and thus probably should be anticoagulated).



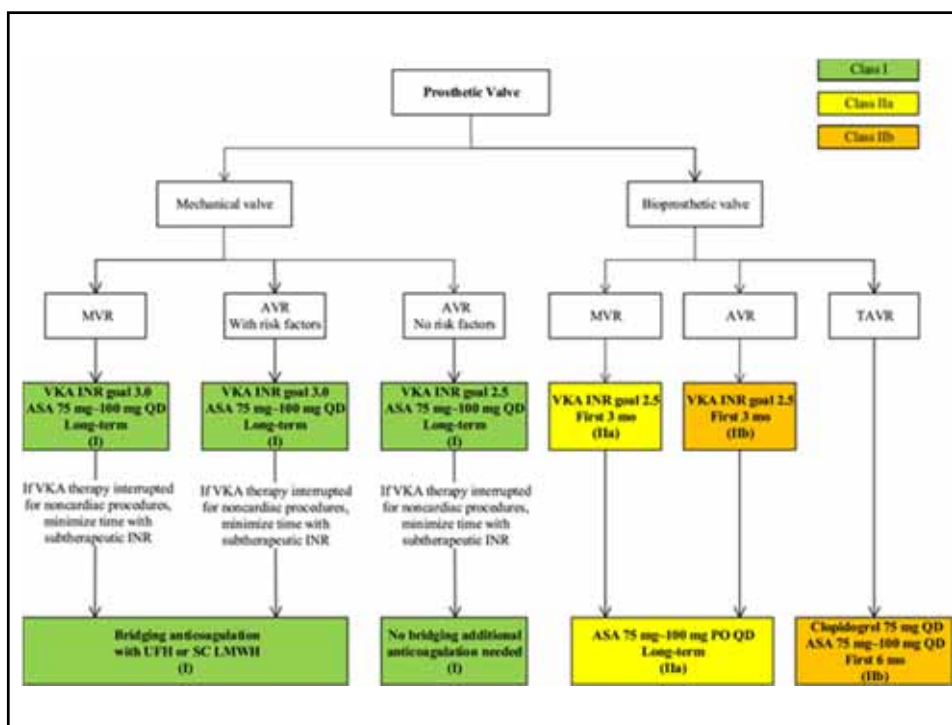
Kovacs et al. *J Am Coll Cardiol.* 2015;65(13):1340-1360.

## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- **Antithrombotic therapy (cont.)**
  - **Additional recommendations:**
    - For lone AF (<60 y/o and no heart disease), ASA or no antithrombotic therapy is acceptable.
    - Regardless of CHA<sub>2</sub>DS<sub>2</sub>-VASc score, anticoagulation is recommended for patients with AF and:
      - Hypertrophic cardiomyopathy
      - Mitral stenosis
      - Mechanical and bioprosthetic valve prostheses

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## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

“Risk factors” on previous slide include:

- Atrial fibrillation
- Previous thromboembolism
- LV dysfunction
- Hypercoagulable condition
- Older-generation mechanical valve prosthesis



## Atrial Fibrillation Anticoagulation

### HAS-BLED Risk Stratification Scheme

Risk Factors	Score
<b>H</b> Hypertension	1
<b>A</b> Abnormal renal and/or liver function (1 point each)	1 or 2
<b>S</b> Stroke	1
<b>B</b> Bleeding predisposition	1
<b>L</b> Labile INR's	1
<b>E</b> Elderly (Age > 65)	1
<b>D</b> Drugs and/or alcohol usage	1 or 2



Pisters et al. *Chest*. 2010;138:1093-1100.

## Atrial Fibrillation Anticoagulation

**HAS-BLED Risk Stratification Scheme (cont.)**

<b>Risk Factor Specifics</b>	<b>Score</b>
<b>H</b> Uncontrolled hypertension (systolic BP > 160 mmHg)	1
<b>A</b> Abn. renal function (dialysis, transplant, Cr > 2.6 mg/dL) Abn. liver function (cirrhosis, bilirubin > 2 x NL, AST/ALT/AP > 3 x NL)	1 or 2
<b>S</b> Stroke history	1
<b>B</b> Prior major bleeding or predisposition to bleeding	1
<b>L</b> Unstable/high INR's, time in therapeutic range < 60%	1
<b>E</b> Elderly (Age > 65)	1
<b>D</b> Drugs (medication usage predisposing to bleeding (antiplatelet agents, NSAID's)) and/or alcohol usage ( $\geq 8$ drinks/week)	1 or 2

Pisters et al. *Chest*. 2010;138:1093-1100.

## Atrial Fibrillation Anticoagulation

**HAS-BLED Risk Stratification Scheme (cont.)**

- **“In patients with a HAS-BLED score  $\geq 3$ , caution and regular review are recommended, as well as efforts to correct the potentially reversible risk factors for bleeding.”**
- **“A high HAS-BLED score *per se* should not be used to exclude patients from oral anticoagulant therapy.”**

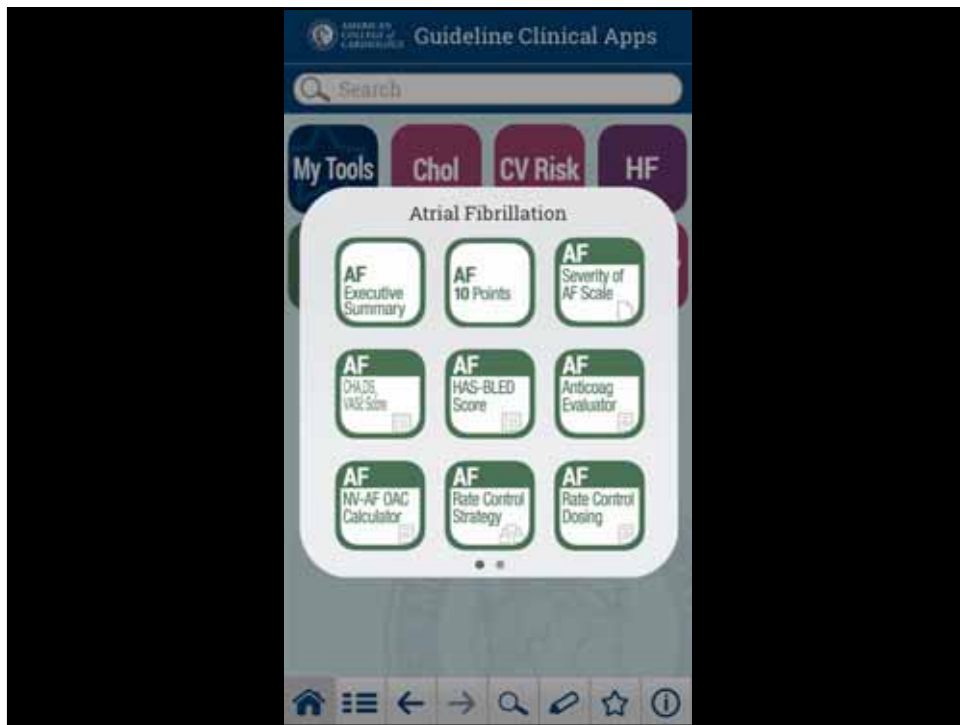
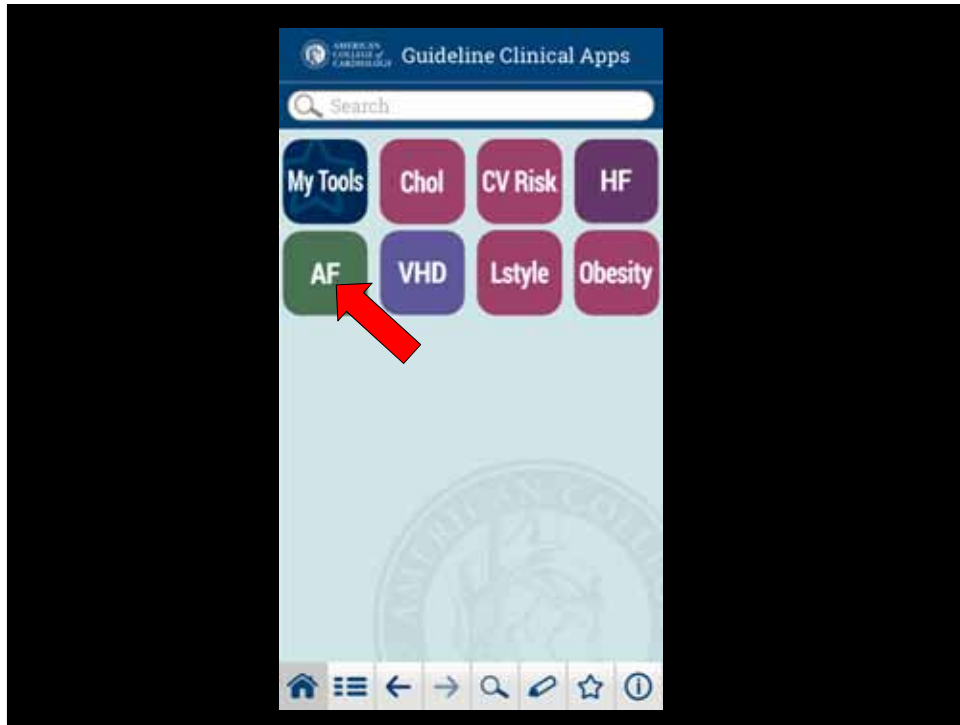
Pisters et al. *Chest*. 2010;138:1093-1100.

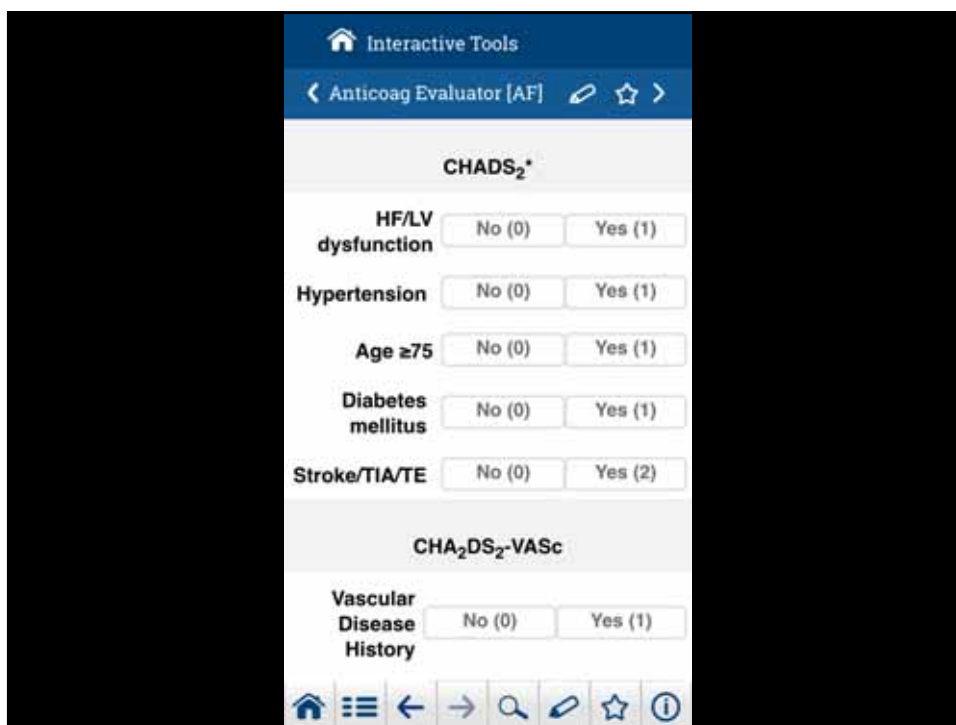
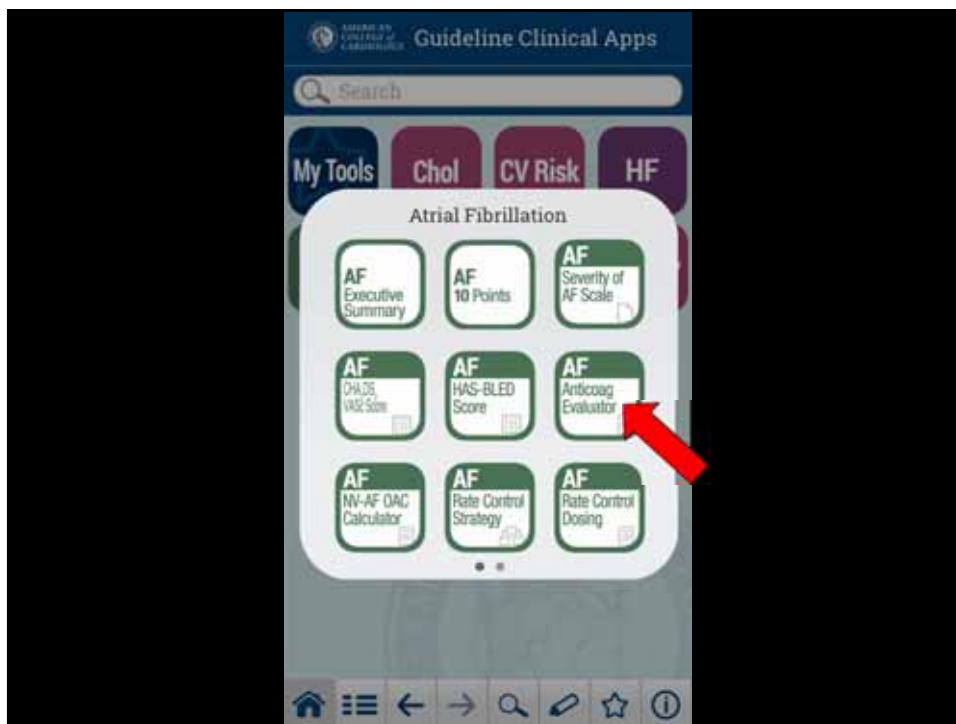
Atrial Fibrillation Anticoagulation

## Treatment Strategy / Options (cont.)

- Antithrombotic therapy (cont.)
  - There's an app for that!
    - Enter: "ACC Guideline Clinical Apps"









Interactive Tools

< Anticoag Evaluator [AF] >

**CHA<sub>2</sub>DS<sub>2</sub>-VASc**

Vascular Disease History

Age 65-74

Sex

**HAS-BLED**

Abnormal RF<sup>2</sup>

Abnormal LF<sup>3</sup>

Bleeding<sup>4</sup>

Home navigation icons: Home, Menu, Back, Forward, Search, Edit, Star, Info

Interactive Tools

< Anticoag Evaluator [AF] >

**HAS-BLED**

Abnormal RF<sup>2</sup>

Abnormal LF<sup>3</sup>

Bleeding<sup>4</sup>

Labile INR<sup>5</sup>

Medication<sup>6</sup>

Alcohol or Drug Usage History<sup>7</sup>

Score (must answer all questions)

Home navigation icons: Home, Menu, Back, Forward, Search, Edit, Star, Info

Interactive Tools

< Anticoag Evaluator [AF] >

CHADS<sub>2</sub>\*: 1

CHA<sub>2</sub>DS<sub>2</sub>-VASc: 2

HAS-BLED: 3

Choice of Therapy† RIVAROXABAN 20 mg onx

Risks/Benefits‡

Patient's ANNUAL risk of ischemic stroke+thromboembolism with rivaroxaban (based on CHADS<sub>2</sub>) 1.2%

Relative risk reduction 66%

Absolute risk reduction 2.4%

Interactive Tools

< Anticoag Evaluator [AF] >

Patient's ANNUAL risk of ischemic stroke+thromboembolism with rivaroxaban (based on CHADS<sub>2</sub>) 1.2%

Relative risk reduction 66%

Absolute risk reduction 2.4%

Chance of benefit per year 1 in 41

Patient's ANNUAL risk of ischemic stroke+thromboembolism with rivaroxaban (based on CHA<sub>2</sub>DS<sub>2</sub>-VASc) 1.0%

Relative risk reduction 66%

Absolute risk reduction 1.9%

Interactive Tools

< Anticoag Evaluator [AF] >

Patient's ANNUAL risk of ischemic stroke+thromboembolism with rivaroxaban (based on CHA<sub>2</sub>DS<sub>2</sub>-VASc) 1.0%

Relative risk reduction 66%

Absolute risk reduction 1.9%

Chance of benefit per year 1 in 52

ANNUAL risk of major bleed (population avg) 3.8%

Chance of being harmed by rivaroxaban (per year, major bleeding, vs. no therapy) 1 in 31

Patient's ANNUAL risk of major bleed (HAS-BLED) 5.6%

Chance of being harmed by rivaroxaban (per year, major bleeding, vs. no therapy) 1 in 20

Interactive Tools

< Anticoag Evaluator [AF] >

ANNUAL risk of major bleed (population avg) 3.8%

Chance of being harmed by rivaroxaban (per year, major bleeding, vs. no therapy) 1 in 31

Patient's ANNUAL risk of major bleed (HAS-BLED) 5.6%

Chance of being harmed by rivaroxaban (per year, major bleeding, vs. no therapy) 1 in 20

**Selected Therapy**

Drug: Rivaroxaban (Xarelto®)

Dose Form: Oral

Recommended Dose: 20 mg daily with evening meal

Renal Impairment

## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants**
  - **Warfarin**
  - **Dabigatran**
  - **Rivaroxaban**
  - **Apixaban**
  - **Edoxaban**

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## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Warfarin (Coumadin<sup>®</sup>, Jantoven<sup>®</sup>)**
    - **Inhibits formation of the reduced form of vitamin K**
    - **Long half-life (37 hours)**
      - **Delayed onset of anticoagulation: 2-7 days**
    - **Variability in warfarin's anticoagulant effect**
      - **Dietary variations in vitamin K content**
      - **Many drug interactions**
  - **Requires monitoring of PT/INR**

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**Atrial Fibrillation Anticoagulation****Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Dabigatran (Pradaxa<sup>®</sup>)**
    - *Oral* direct thrombin inhibitor
      - At least as effective as warfarin (in reducing the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation), without increased bleeding risk
    - No monitoring of coagulation studies needed
    - No dietary restrictions
    - Minimal drug interactions

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HEALTH**Atrial Fibrillation Anticoagulation****Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Dabigatran (cont.)**
    - Dose reduction necessary in renal insufficiency
    - Antidote now available: idarucizumab (Praxabind<sup>®</sup>)

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Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Rivaroxaban (Xarelto®)**
    - *Oral* factor Xa inhibitor
    - Does *not* bind to antithrombin III
    - Once daily dosing
    - Dose reduction necessary in renal insufficiency



The only once-daily, fixed-dose anticoagulant to reduce stroke risk in nonvalvular AF patients—

**PROTECTION IN ACTION...**



ONCE-DAILY  
**Xarelto®**  
rivaroxaban tablets  
APPROVED FOR MULTIPLE INDICATIONS

## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Apixaban (Eliquis®)**
    - *Oral* factor Xa inhibitor
    - Does *not* bind to antithrombin III
    - Twice daily dosing



## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Apixaban (cont.)**
    - **Dose reduction necessary in patients with at least two of the following:**
      - Age  $\geq$  80 years
      - Weight  $\leq$  60 kg
      - Serum Cr  $\geq$  1.5 mg/dL



## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants (cont.)**
  - **Edoxaban (Savaysa®)**
    - *Oral* factor Xa inhibitor
    - Does *not* bind to antithrombin III
    - Once daily dosing
    - Dose reduction necessary in renal insufficiency
    - Avoid use if CrCl > 95 ml/min.

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## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- **Oral anticoagulants – *memory aid*:**
  - Warfarin
  - Dabigatran
  - Rivaroxaban
  - Apixaban
  - Edoxaban

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## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- Oral anticoagulants – *memory aid*:
  - Warfarin
  - **D**abigatran
  - Rivarox**a**ban
  - Apix**a**ban
  - Edox**a**ban



## Atrial Fibrillation Anticoagulation

**Treatment Strategy / Options (cont.)**

- Oral anticoagulants – *memory aid*:
  - Warfarin
  - **D**abigatran: **D**irect thrombin inhibitor
  - Rivarox**a**ban: Factor **Xa** inhibitor
  - Apix**a**ban: Factor **Xa** inhibitor
  - Edox**a**ban: Factor **Xa** inhibitor



## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- **Oral anticoagulants – *memory aid*:**
  - **Warfarin:** Vitamin K antagonist
  - **Dabigatran:** Direct thrombin inhibitor
  - **Rivaroxaban:** Factor Xa inhibitor
  - **Apixaban:** Factor Xa inhibitor
  - **Edoxaban:** Factor Xa inhibitor



## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- **Temporary interruption of oral anticoagulant therapy for invasive procedures:**
  - For nonvalvular atrial fibrillation, short-term interruption of oral anticoagulant therapy is safe for most low-risk invasive procedures.
  - For patients at higher thromboembolic risk who are undergoing high risk procedures, “bridging” with a parenteral anticoagulant becomes a stronger consideration.



## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- Temporary interruption of oral anticoagulant therapy for invasive procedures (cont.):
  - Warfarin
    - Number of days warfarin must be withheld prior to procedure depends on that individual's usual maintenance dose
    - Check INR prior to procedure to assure subtherapeutic level
  - Dabigatran
    - If  $CrCl \geq 50$  ml/min, stop dabigatran at least 1-2 days prior to procedure
    - If  $CrCl < 50$  ml/min, stop dabigatran at least 3-5 days prior to procedure

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## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- Temporary interruption of oral anticoagulant therapy for invasive procedures (cont.):
  - Apixaban
    - For moderate-high-bleeding risk procedures, stop apixaban at least 48 hours prior to the procedure.
    - For low bleeding-risk procedures, stop apixaban at least 24 hours prior to the procedure.
  - Rivaroxaban & edoxaban
    - Stop rivaroxaban and edoxaban at least 24 hours prior to the procedure.

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## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- **Dosing considerations for oral anticoagulants in nonvalvular atrial fibrillation:**
  - **Warfarin**
    - One (of two) oral anticoagulants that may be used in patients with severe renal dysfunction or end-stage renal disease (which is the other?)
    - Caution in patients with moderate-to-severe hepatic impairment.
  - **Dabigatran**
    - If CrCl > 30 ml/min, dose is 150 mg PO BID
    - If CrCl is 15-30 ml/min, dose is 75 mg PO BID
    - If CrCl < 15 ml/min, avoid use

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## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- **Dosing considerations for oral anticoagulants in nonvalvular atrial fibrillation (cont.):**
  - **Apixaban**
    - Usual dose is 5 mg PO BID, unless the patient has at least two of the following (in which case the recommended dose is 2.5 mg PO BID):
      - Age  $\geq$  80 years
      - Weight  $\leq$  60 kg
      - Serum Cr  $\geq$  1.5 mg/dL
    - Is the other of the two oral anticoagulants that may be used in patients with severe renal dysfunction or end-stage renal disease

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## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- Dosing considerations for oral anticoagulants in nonvalvular atrial fibrillation (cont.):
  - Apixaban (cont.)
    - “For nonvalvular AF patients with ESRD maintained on hemodialysis, the recommended dose is 5 mg PO BID”
    - Reduce dose to 2.5 mg PO BID if the patient has at least one of the following:
      - Age  $\geq$  80 years
      - Weight  $\leq$  60 kg



## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- Dosing considerations for oral anticoagulants in nonvalvular atrial fibrillation (cont.):
  - Rivaroxaban
    - If CrCl > 50 ml/min, dose is 20 mg PO daily
    - If CrCl is 15-50 ml/min, dose is 15 mg PO daily
    - If CrCl < 15 ml/min, avoid use
  - Edoxaban
    - If CrCl is 51-95 ml/min, dose is 60 mg PO daily
    - If CrCl is 15-50 ml/min, dose is 30 mg PO daily
    - If CrCl > 95 ml/min, avoid use



## Atrial Fibrillation Anticoagulation

### Treatment Strategy / Options (cont.)

- **Special circumstance worth noting...**
  - After coronary revascularization, in patients with nonvalvular AF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score > 1, current consensus is that “it may be reasonable to use clopidogrel concurrently with oral anticoagulants but without aspirin.”



## Cardiovascular Case for questions 1 & 2

### Use the following case for the next two questions:

A 46-year-old female presents for preoperative evaluation prior to elective total abdominal hysterectomy. Her medical history is significant for endometriosis, hypertension, and paroxysmal atrial fibrillation. An echocardiogram performed last month revealed normal left ventricular systolic function, mild tricuspid regurgitation, trace mitral regurgitation, and no significant structural abnormalities. Her medications include warfarin 2 mg PO daily and atenolol 25 mg PO BID. Her INR is 2.8. The remainder of her lab work (CBC and CMP) is within normal limits. Physical examination reveals: blood pressure 126/82 mmHg, pulse 80 bpm, and respirations 12 per min. There is no jugular venous distension, lungs are clear to auscultation bilaterally (no crackles or wheezes), cardiac rhythm is regular and there is no S3, S4, murmur, or rub. There is no peripheral edema.



## Cardiovascular Case-1

### Question 1

Which of the following is the most appropriate recommendation regarding anticoagulation prior to surgery?

- A. Discontinue warfarin now, as anticoagulation is not indicated in this patient.
- B. Discontinue warfarin four days prior to scheduled surgery. Check the INR daily. When the INR is  $< 2$ , begin enoxaparin 1 mg/kg SQ BID and continue it until the morning of surgery.
- C. Discontinue warfarin four days prior to scheduled surgery. Check the INR the morning of scheduled surgery. Proceed with surgery if the INR is  $< 2$ .
- D. Continue warfarin through the day before scheduled surgery. Withhold warfarin on the morning of surgery and initiate a continuous intravenous infusion of unfractionated heparin, which may then be discontinued on call to the operating room.



## Cardiovascular Case-1

### Question 2

Provided that the surgery was uneventful, which of the following is the most appropriate recommendation regarding anticoagulation postoperatively?

- A. Do not resume anticoagulation postoperatively, as it is not indicated in this patient.
- B. Resume warfarin as soon as the surgeon feels that the patient is at a low risk for bleeding. Discharge the patient when the INR is  $\geq 2$ .
- C. Begin enoxaparin 1 mg/kg SQ BID and resume warfarin 2 mg PO daily as soon as the surgeon feels that the patient is at a low risk for bleeding. Check the INR daily. Discontinue enoxaparin and discharge the patient when the INR is  $\geq 2$ .
- D. Begin enoxaparin 1 mg/kg SQ BID and resume warfarin 2 mg PO daily as soon as the surgeon feels that the patient is at a low risk for bleeding. Check the INR daily until the INR is  $\geq 2$ . Discontinue enoxaparin after 10 doses regardless of INR.



### Cardiovascular Case for questions 3 & 4

#### Use the following case for the next two questions:

A 66-year-old male presents for preoperative evaluation prior to elective total right knee arthroplasty. His medical history is significant for DJD, type II diabetes mellitus, and paroxysmal atrial fibrillation. An echocardiogram performed three months ago revealed mild left ventricular systolic dysfunction (LVEF 45%), mild mitral regurgitation, trace tricuspid regurgitation, and mild thickening of the aortic valve without stenosis. His medications include rivaroxaban 20 mg PO daily, metformin 500 mg PO BID, sitagliptin 100 mg PO daily, metoprolol 25 mg PO BID, and acetaminophen 650 mg PO q 6 hrs. PRN pain. His preoperative lab work (including PT/INR, CBC, and CMP) are within normal limits. Physical examination reveals: Temperature 97.8°F, blood pressure 122/76 mmHg, pulse 68 bpm, and respirations 14 per min. There is no jugular venous distension, lungs are clear to auscultation bilaterally, cardiac rhythm is regular, a soft S4 is present, and there is no S3. A grade 2/6 pansystolic murmur is heard at the cardiac apex. Abdominal exam is unremarkable. With the exception of mild swelling of the right knee, there is no peripheral edema.

### Cardiovascular Case 2

#### Question 3

Which of the following is the most appropriate recommendation regarding anticoagulation prior to surgery?

- Discontinue rivaroxaban now, as anticoagulation is not indicated in this patient.
- Discontinue rivaroxaban 48 hours prior to scheduled surgery. Begin enoxaparin 1 mg/kg SQ BID 24 hours after the last rivaroxaban dose. Discontinue enoxaparin on the morning of surgery.
- Discontinue rivaroxaban 48 hours prior to scheduled surgery. Order a factor Xa inhibition assay on the morning of scheduled surgery. Proceed with surgery if the assay reveals subtherapeutic factor Xa inhibition.
- Discontinue rivaroxaban 48 hours prior to scheduled surgery.





## Cardiovascular Case 2

### Question 4

Provided that the surgery was uneventful, which of the following is the most appropriate recommendation regarding anticoagulation postoperatively?

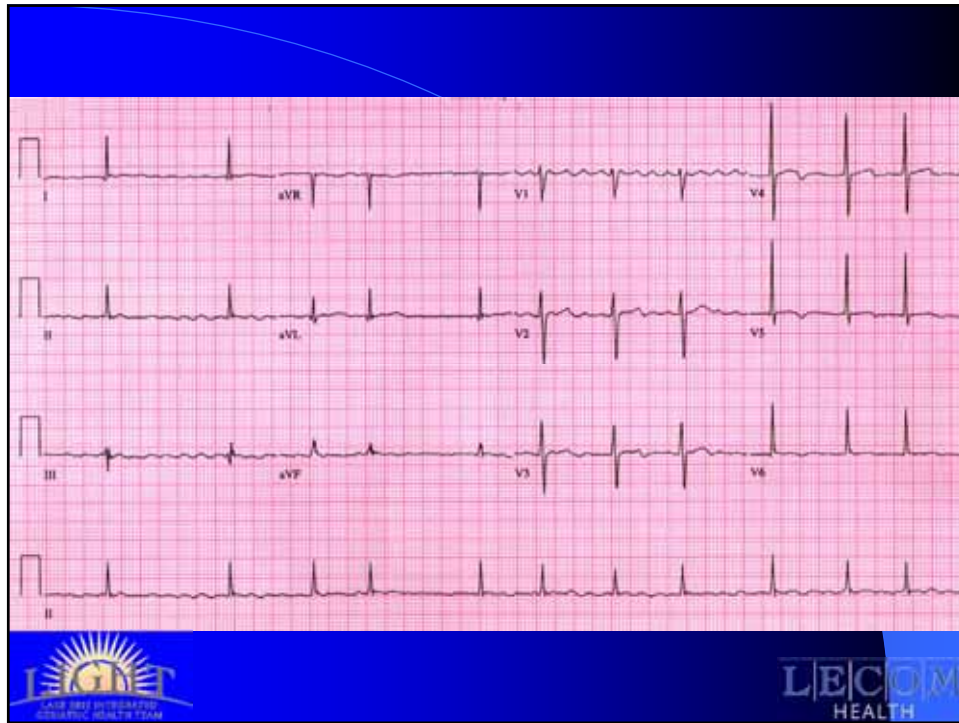
- A. Do not resume anticoagulation postoperatively, as it is not indicated in this patient.
- B. Resume rivaroxaban 20 mg PO daily as soon as the surgeon feels that the patient is at a low risk for bleeding. Obtain a factor Xa inhibition assay daily after resuming rivaroxaban. Discharge the patient when the assay reveals therapeutic factor Xa inhibition.
- C. Begin enoxaparin 1 mg/kg SQ BID and resume rivaroxaban 20 mg PO daily as soon as the surgeon feels that the patient is at a low risk for bleeding. Discontinue enoxaparin after four days, as it takes five half-lives to achieve steady state with rivaroxaban.
- D. Resume rivaroxaban 20 mg PO daily as soon as the surgeon feels that the patient is at a low risk for bleeding.



## Cardiovascular Case 3

### Case Presentation 3

A 53-year-old male presents to his primary care physician's office for a scheduled routine medical evaluation. He denies any symptoms or recent problems, and he states that he feels fine. His medical history is significant for coronary artery disease (having undergone implantation of a drug-eluting stent into the proximal LAD four months ago), hypertension, and hyperlipidemia. An echocardiogram performed one week after LAD stenting revealed normal left ventricular systolic function (LVEF 55%), mild mitral regurgitation, mild tricuspid regurgitation, moderate left atrial dilatation, and no other significant structural abnormalities. His current medications include aspirin 81 mg PO daily, clopidogrel 75 mg PO daily, atorvastatin 80 mg PO daily, metoprolol ER 100 mg PO daily, and ramipril 5 mg PO daily. Vital signs are: temperature 98.4 F, blood pressure 124/78 mmHg, pulse 68 bpm, and respirations 12 per min. The remainder of the physical examination is unremarkable except for an irregularly irregular rhythm, and a grade 2/6 pansystolic murmur heard along the lower left sternal border and at the cardiac apex. A 12-lead electrocardiogram is obtained (see next slide).



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#### Question 5

Which of the following is the most appropriate recommendation regarding antithrombotic therapy for this patient?

- A. Continue aspirin and clopidogrel, without adding an oral anticoagulant.
- B. Continue aspirin and clopidogrel, and begin oral anticoagulant therapy.
- C. Continue aspirin, discontinue clopidogrel, and begin oral anticoagulant therapy.
- D. Continue clopidogrel, discontinue aspirin, and begin oral anticoagulant therapy.
- E. Discontinue both antiplatelet agents, and begin oral anticoagulant therapy.