

A scenic view of the Golden Gate Bridge in San Francisco, California, with a dog running on a beach in the foreground. The bridge is a prominent red-orange suspension bridge spanning the water. The beach is dark sand, and the dog is a fluffy, light-colored breed. The sky is clear and blue.

# Update on the Management of the Hospitalized Patient with Atrial Fibrillation

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Professor of Medicine  
Division of Cardiology  
University of California, San Francisco

# Disclosures

## Research:

- NIH
- PCORI
- Baylis
- Eight Sleep
- Jawbone
- Medtronic

## Consulting and Equity:

- InCarda

# Relevant Advances in Atrial Fibrillation

- What evaluation does one need to do?
- What is the first line treatment?
- What about all these anticoagulation options?
- What is the rationale for rhythm control?

# Epidemiology

- AF is the most common sustained arrhythmia in adults
- Affects ~4% of everyone over age 60 and ~10% of everyone over age 80
- The age-adjusted incidence is increasing<sup>1</sup>

# My patient has AF

## What work-up do I need to do?

**Circulation**

JOURNAL OF THE AMERICAN HEART ASSOCIATION



**American  
Heart  
Association®**

**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**

Craig T. January, L. Samuel Wann, Joseph S. Alpert, Hugh Calkins, Joseph C. Cleveland, Jr, Joaquin E. Cigarroa, Jamie B. Conti, Patrick T. Ellinor, Michael D. Ezekowitz, Michael E. Field, Katherine T. Murray, Ralph L. Sacco, William G. Stevenson, Patrick J. Tchou, Cynthia M. Tracy and Clyde W. Yancy

*Circulation.* published online March 28, 2014;

- Diagnosis by ECG
- Transthoracic Echocardiogram
- Electrolytes, TFTs, creatinine, hepatic function and blood count

# My patient has AF

## What work-up do I need to do?

- What about a troponin?
- What about a VQ scan or CT angio?

# What is the first thing I need to do?

- RATE CONTROL
  - If unstable → DC shock
- Your favorite beta-blocker or calcium channel blocker
- When BP goes down:
  - Consider MORE AV nodal blockage
  - Consider Dig
  - Consider amiodarone
  - Consider esmolol
  - Consider cardioversion

# What is the first thing I need to do? Can they go home?

- Remember a lot of these people are walking around or coming to clinic with fast heart rates
- Dictated primarily by symptoms and how stable they are
- Tachy cardiomyopathy **DOES HAPPEN**
  - Likely after a few weeks at  $>120$  or so



# Atrial Fibrillation and Stroke

- AF is the most common cause of embolic stroke<sup>1</sup>
- 15% of all strokes in the US can be attributed to AF<sup>1</sup>
- AF is associated with an increase in mortality, from 1.3-2 times<sup>2</sup>

1. Nattel. Lancet 2006;367:262-272

2. Page. N Engl J Med 2004;351:2408-16

# Atrial Fibrillation and Other Bad Things

- AF increases risk of:
  - Heart failure<sup>1</sup>
  - Dementia<sup>2</sup>

1. Wang et al. Circulation 2003; 107:2920-5
2. Ott et al. Stroke 1997;28:316-21.

# Atrial Fibrillation and Other Bad Things

**Circulation**  
JOURNAL OF THE AMERICAN HEART ASSOCIATION



## **Incident Atrial Fibrillation and Risk of End-Stage Renal Disease in Adults With Chronic Kidney Disease**

Nisha Bansal, Dongjie Fan, Chi-yuan Hsu, Juan D. Ordonez, Greg M. Marcus and Alan S. Go

*Circulation.* 2013;127:569-574; originally published online December 28, 2012;

**Table 2. Association Between Incident Atrial Fibrillation and Subsequent Risk of End-Stage Renal Disease Among Adults With Chronic Kidney Disease**

	HR (95% CI)
Unadjusted	1.18 (1.06–1.31)
Adjusted for patient characteristics, cardiovascular risk factors, and medication use*	1.67 (1.46–1.91)

# Atrial Fibrillation and Other Bad Things

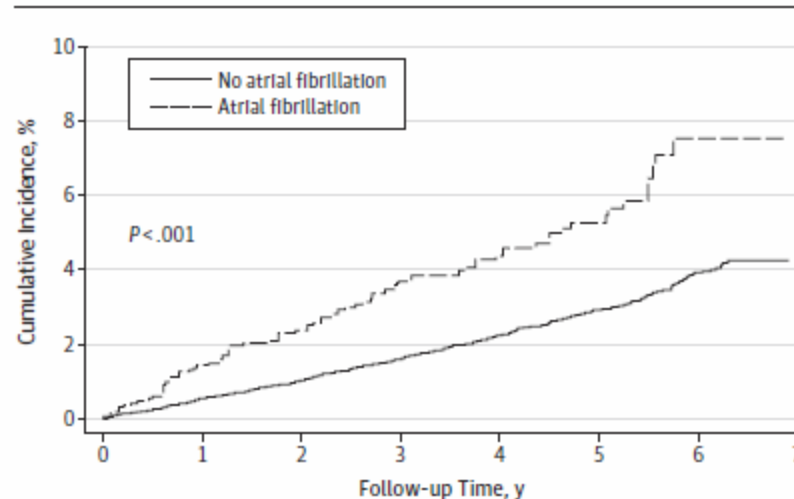
Original Investigation

## Atrial Fibrillation and the Risk of Myocardial Infarction

Elsayed Z. Soliman, MD, MSc, MS; Monika M. Safford, MD; Paul Muntner, PhD; Yulia Khodneva, MD, PhD; Farah Z. Dawood, MD; Neil A. Zakai, MD; Evan L. Thacker, PhD; Suzanne Judd, PhD; Virginia J. Howard, PhD; George Howard, DrPH; David M. Herrington, MD, MHS; Mary Cushman, MD, MSc

JAMA Internal Medicine Published online November 4, 2013

Figure 1. Unadjusted Cumulative Incidence of Myocardial Infarction by Baseline Atrial Fibrillation Status



# Audience Response Question Among Cryptogenic Stroke Patients, AF can be found in:

- 0-3%
- 3-10%
- 10-20%
- 20-30%

## Cryptogenic Stroke and Underlying Atrial Fibrillation

- 12.4% of cryptogenic stroke patients discovered to have AF via an implantable loop recorder
  - Versus 2% in those with usual care
- AF can be and is often asymptomatic!

# Injectable Loop Recorder



- It is MRI compatible once it has been in for ~1 month

# Anticoagulation in AF

- **Warfarin has been the most effective available therapy to prevent stroke in patients with AF**
  - 5 RCT of vit K antagonists v. placebo highly significant risk reduction in stroke of 62% (95% CI 48% to 72%)<sup>1</sup>
  - Strokes on warfarin are significantly less severe<sup>2</sup>
  - Warfarin reduced overall mortality in AF patients<sup>3</sup>

1. Ann Intern Med 1999;131:492-501

2. Chest 2004;126:429S-456S)

3. Eur Heart J 2005;7:C12-18



# Anticoagulation in AF

- **Warfarin is not perfect**
  - Significantly increase major bleeding (0.9% to 2.2%) and intracerebral hemorrhage (0.2% to 0.4%)<sup>1</sup>

1. Eur Heart J 2005;7:C12-18

# Novel anticoagulants

- Predictable pharmacokinetics
  - Do not require monitoring, frequent blood draws
  - Do not require dose adjustments
- Do not take several days onset and offset
  - Directly inhibits thrombin/ Xa, so may not require bridging
- No food interactions
  - Not related to vitamin K, so no known important food interactions

# Novel anticoagulants

- Dabigatran = Pradaxa
- Rivaroxaban = Xarelto
- Apixiban = Eliquis
- Savaysa = Edoxaban

# Audience Response Question

The Four Randomized Trials of the Novel Anticoagulation Drugs versus Warfarin included:

- 994, 1,032, 1,068, and 3,200 participants
- 4,540, 4,895, 5,352, and 6,105 participants
- 7,511, 7,965, 9,003, and 9,423 participants
- 10,055, 12,607, 12,934, and 13,544 participants
- 14,264, 18,113, 18,201, and 21,105 participants

The NEW ENGLAND  
JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 17, 2009

VOL. 361 NO. 12

Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.D., Philip Alimi, M.D., Philip A. Alimi, M.D., John Eikelboom, M.D., Jonas Oldgren, M.D., Ph.D., Amit Parekh, M.D., Janice Pogue, M.Sc., Paul A. Reilly, Ph.D., Ellison Themeles, B.A., Jeanne Varrone, M.D., Susan Wang, Ph.D., Marco Alings, M.D., Ph.D., Denis Xavier, M.D., Jun Zhu, M.D., Rafael Diaz, M.D., Basil S. Lewis, M.D., Harald Darius, M.D., Hans-Christoph Diener, M.D., Ph.D., Campbell D. Joyner, M.D., Lars Wallentin, M.D., Ph.D., and the RE-LY Steering Committee and Investigators\*

N=18,113

ORIGINAL ARTICLE

Rivaroxaban versus Warfarin in Nonvalvular  
Atrial Fibrillation

Manesh R. Patel, M.D., Kenneth W. Mahaffey, M.D., Jyotsna Garg, M.S., John F. Paolillo, Ph.D., Michael E. Scharf, M.D., Robert M. Califf, M.D., Joseph A. DeGroot, M.D., Jonathan Halperin, M.D., Gregory H. Yip, M.D., John F. Paolillo, M.D., Ph.D., Keith A.A. Fox, M.B., Ch.B., Robert M. Califf, M.D., and the ROCKET AF Steering Committee, for the ROCKET AF Investigators\*

N=14,264

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SEPTEMBER 15, 2011

VOL. 365 NO. 11

Apixaban versus Warfarin in Patients  
with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., John J.V. Moore, M.D., Stefano D. Jolly, M.D., Ph.D., Elaine M. Hylek, M.D., Philip A. Alimi, M.D., Al-Kharrat, Ph.D., Atar, M.D., Al-Kharrat, M.D., M. Cecilia B. de Souza, M.D., Rafael Diaz, M.D., Jonathan Halperin, M.D., Justin E. Ezekowitz, M.D., Greg Alker, M.D., David Garcia, M.D., Mauricio G. Andrade, Ph.D., Bernard Gersh, M.D., Sergey Golitsyn, M.D., Antonio G. Hermida, M.D., Stefan H. Hohnloser, M.D., John Horowitz, M.D., Puneet Mohan, M.D., Ph.D., Petr Jansky, M.D., Basil S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Prem Pais, M.D., Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D., and Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators\*

N=18,201

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2013;369:2093-104.

ORIGINAL ARTICLE

Edoxaban versus Warfarin in Patients  
with Atrial Fibrillation

Robert P. Giugliano, M.D., Christian T. Ruff, M.D., M.P.H., Eugene Braunwald, M.D., Sabina A. Murphy, M.P.H., Stephen D. Wiviott, M.D., Jonathan L. Halperin, M.D., Albert L. Lloyd, M.D., Michael Ezekowitz, M.D., Philip A. Alimi, M.D., James J. Hanyok, Pharm.D., William D. White, M.D., Philip A. Alimi, M.D., Yukihiko Shimada, M.D., Shuaqun Wu, Ph.D., Mingyi Song, Ph.D., Laura A. Griep, A.B., Paul B. Israel, M.D., and Elliott M. Antman, M.D., for the ENGAGE AF-TIMI 48 Investigators\*

N=21,105

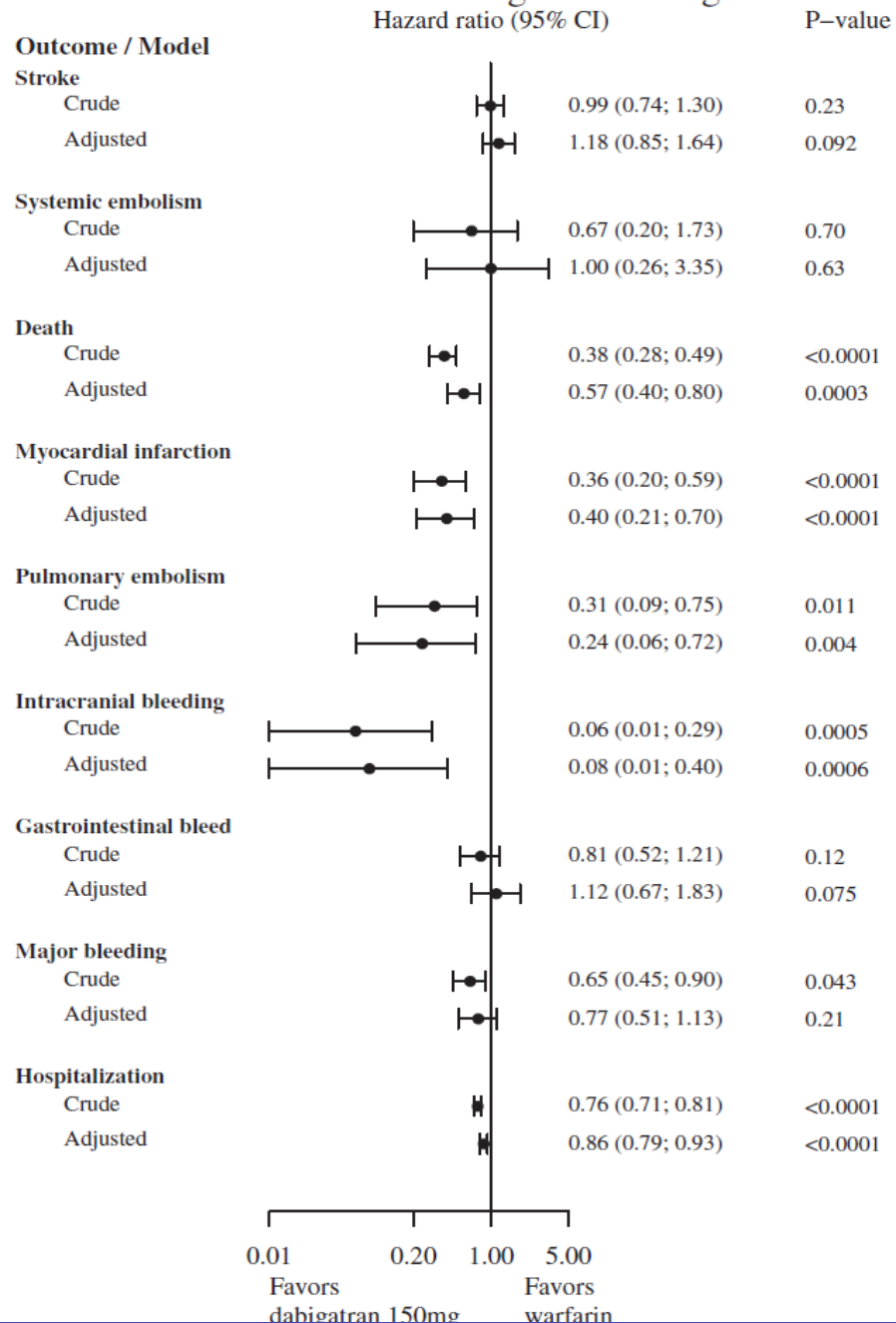
# VERSUS WARFARIN in AF

<b>Drug</b>	<b>Preventing Stroke or Thromboembolism</b>	<b>Bleeding</b>
Dabigatran=Pradaxa	Better	Similar
Rivaroxaban=Xarelto	Similar	Similar
Apixiban=Eliquis	Better	Better
Edoxaban=Savaysa	Similar to better	Better

# VERSUS WARFARIN in AF

<b>Drug</b>	<b>Intracranial bleeding</b>	<b>GI Bleeding</b>
Dabigatran=Pradaxa	Much less	More
Rivaroxaban=Xarelto	Much less	More
Apixiban=Eliquis	Much less	Similar
Edoxaban=Savaysa	Much less	More

# Warfarin vs dabigatran 150mg



- “Real world”
- Dabigatran v warfarin
- Danish Registry
- Propensity matched
- N= >12,000



## **ACC/AHA/HRS GUIDELINE**

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# **2019 AHA/ACC/HRS Focused Update of the 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 Clinical Practice Guidelines and the Heart Rhythm Society**

- Class 1A: NOACs (dabigatran, rivaroxaban, apixaban, edoxaban) are now recommended **OVER** warfarin in NOAC-eligible patients with AF
- NOAC “contra-indication” in “valve disease” clarified: mitral stenosis or mechanical heart valves

# Devices for stroke prevention

- All anticoagulants by nature will be associated with an increased risk of bleeding
- In AF patients with thrombus/thromboembolism, the left atrial appendage is thought to be the site of thrombus formation in more than 90%

## ACC/AHA/HRS GUIDELINE

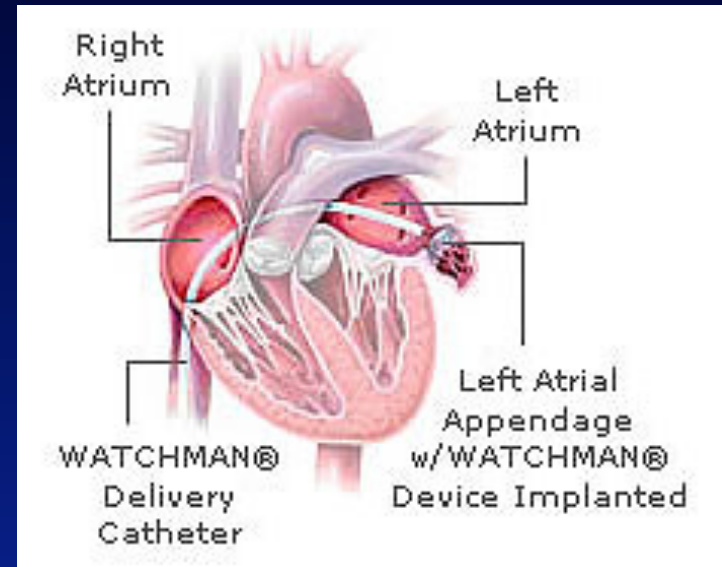
# 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

**Recommendation for Percutaneous Approaches to Occlude the LAA**  
Referenced studies that support the new recommendation are summarized in [Online Data Supplement 4](#).

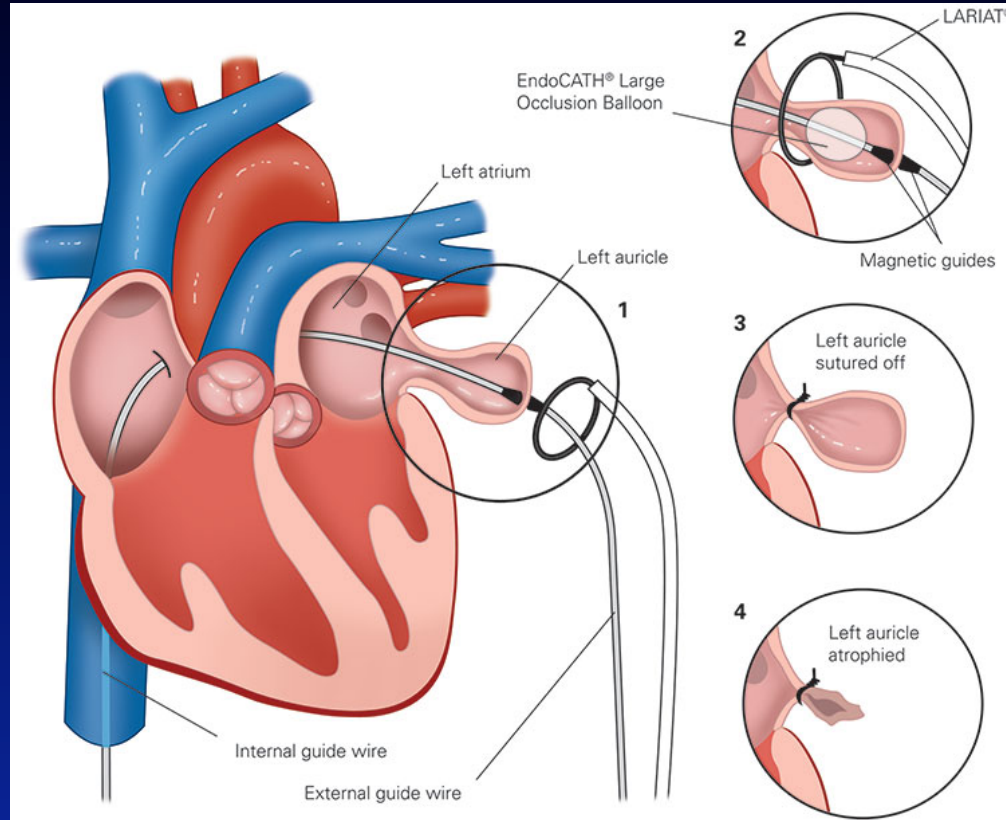
COR	LOE	Recommendation
IIb	B-NR	<p>1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation.<sup>S4.4.1-1–S4.4.1-5</sup></p> <p><b>NEW:</b> Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.</p>

# The Watchman Device is now FDA approved as an alternative to warfarin



A self-expanding nickel titanium (nitinol) frame structure with fixation barbs and a permeable polyester fabric cover implanted via a trans-septal approach to seal the left atrial appendage<sup>1</sup>

# Lariat made by SentreHeart



- No randomized outcomes data
- May be considered if cannot anticoagulate

**Definition and Scores for CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc**

	Score
<b>CHADS<sub>2</sub> acronym</b>	
Congestive HF	1
Hypertension	1
Age ≥75 y	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum Score	6
<b>CHA<sub>2</sub>DS<sub>2</sub>-VASc acronym</b>	
Congestive HF	1
Hypertension	1
Age ≥75 y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65–74 y	1
Sex category (i.e., female sex)	1
Maximum Score	9

# Anticoagulation

- FIRST POINT CLASS 1: Antithrombotic therapy should be individualized based on shared decision making
- Oral anticoagulation for  $\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2$  in men or  $\geq 3$  in women (modified in 2019)

# Anticoagulation

- For patients with nonvalvular AF and a CHA<sub>2</sub>DS<sub>2</sub>-VASc of 0 in men or 1 in women, it is reasonable to omit *antithrombotic* therapy
- What about CHA<sub>2</sub>DS<sub>2</sub>-VASc of 1 in men or 2 in women? → See FIRST POINT ABOVE



# Bridging



# Bridging

- OK to just start warfarin without heparin
- Pharmacokinetics of NOACs can be considered similar to lovenox
- On warfarin:
  - Low risk: can hold for a week
    - For NOACs, should be gone in 2 days
  - High risk (mechanical valve, prior stroke, higher CHA<sub>2</sub>DS<sub>2</sub>-VASc), can consider unfractionated or low molecular weight heparin for warfarin
  - Continue (as is done in many EP procedures)

# Bridging

- On novel agent:
  - Hold for 1 day prior to the procedure (2 doses if BID, 1 dose if QD)
  - When need complete hemostasis (eg, spinal puncture, major surgery), hold for 48 hours
  - Consider continuing (as we now do in many EP procedures)

## ACC/AHA/HRS GUIDELINE

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I	B-NR	<p>3. Idarucizumab is recommended for the reversal of dabigatran in the event of life-threatening bleeding or an urgent procedure.<sup>S4.3-2</sup></p> <p><b>NEW:</b> New evidence has been published about idarucizumab to support LOE B-NR.</p>
IIa	B-NR	<p>4. Andexanet alfa can be useful for the reversal of rivaroxaban and apixaban in the event of life-threatening or uncontrolled bleeding.<sup>S4.3-3,S4.3-4</sup></p> <p><b>NEW:</b> New evidence has been published about andexanet alfa to support LOE B-NR.</p>



“Let’s just cardiovert back to sinus rhythm so we don’t need to worry about anticoagulation.”

# I decide to go with

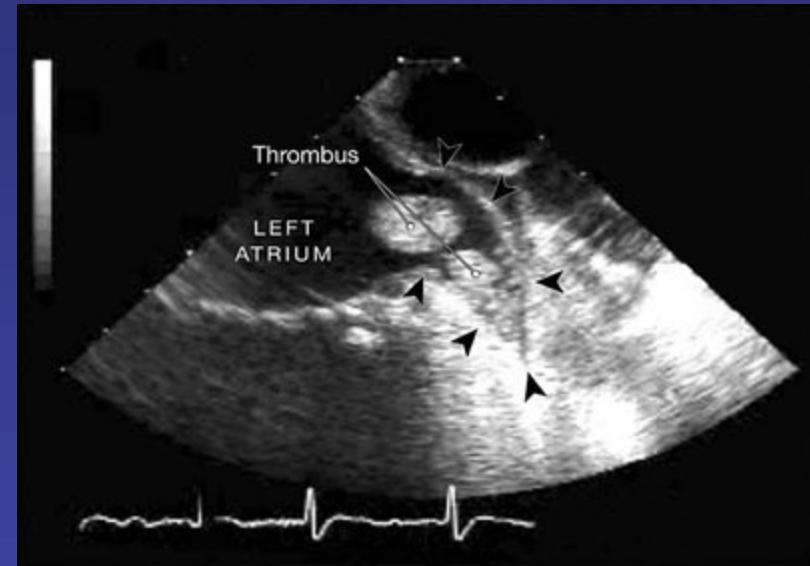


- Cardioversion can reduce left atrial appendage function
  - Even from AF to sinus
- The pericardioversion period is a particularly pro-thrombotic time
  - Regardless of mode: DC/ electrical, pharmacologic, spontaneous

# I decide to go with



- Prior to cardioversion:<sup>1, 2</sup>
  - Can exclude preexisting thrombus by TEE
  - Can anticoagulate (therapeutic/ for at least 3 weeks) prior to cardioversion



1. JACC 2006;48:e149-246
2. Chest 2004;126:429S-456

# I decide to go with



- During and after cardioversion:<sup>1, 2</sup>
  - Anticoagulation for at least 4 weeks
  - Applies even to those who would otherwise not require anticoagulation

1. JACC 2006;48:e149-246

2. Chest 2004;126:429S-456

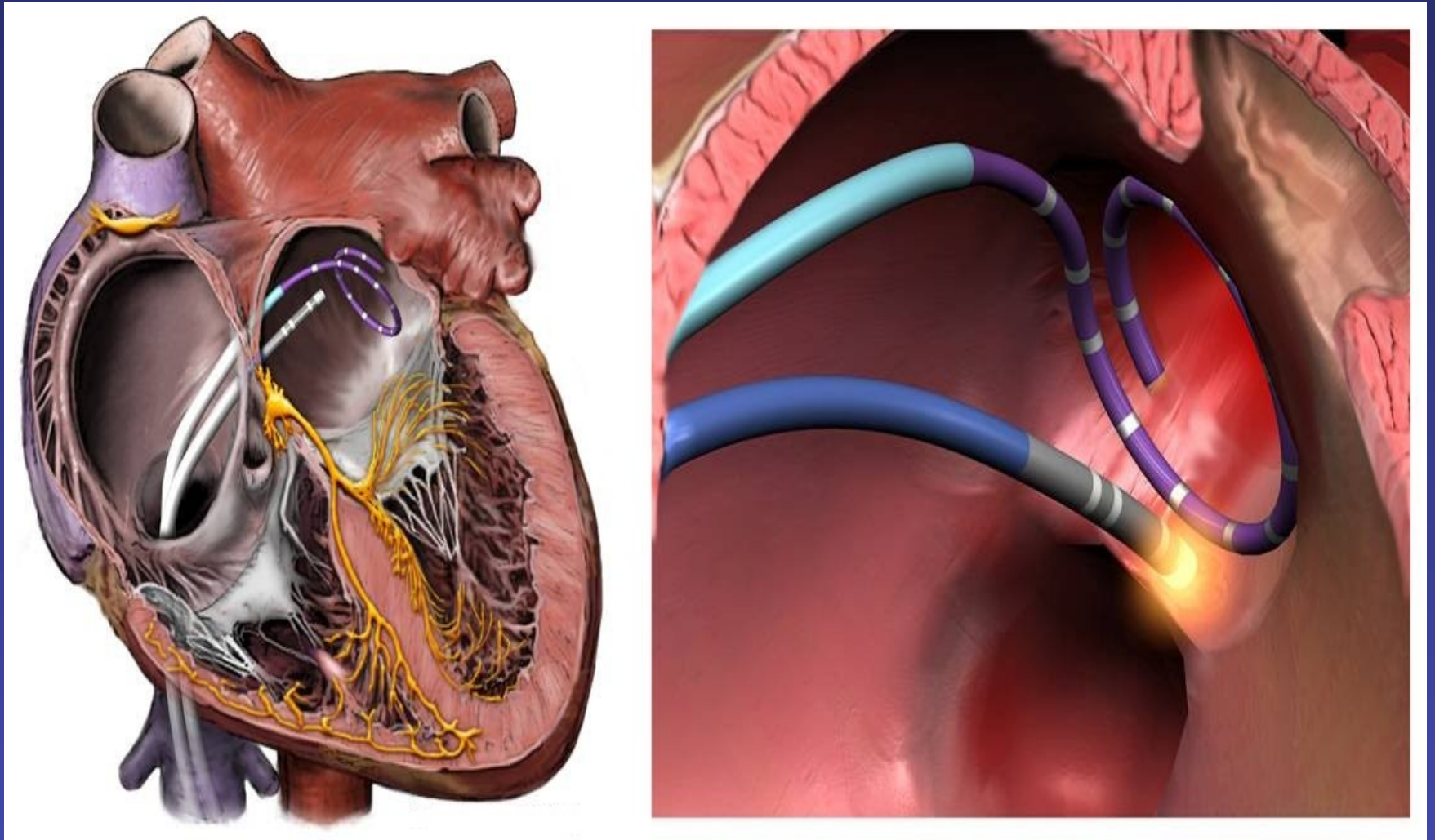


# I decide to go with



- The magic 48 hours
  - Must be documented!
  - Reason to consider starting anticoagulation NOW in the hospital as it may “stop the clock”

# Atrial Fibrillation Ablation



# Atrial Fibrillation Ablation

- High success (> 90-95%) and low risk (< 1%):
  - AV nodal ablation and pacemaker
  - Atrial flutter ablation
  - SVT ablation

# Atrial Fibrillation Ablation

- Lower success (60-90%) and higher risk (4-6%):<sup>1-5</sup>
  - Atrial fibrillation ablation, based primarily on pulmonary vein isolation
- A great option for symptomatic patients
- An ELECTIVE PROCEDURE

1. Circulation 2003;108:2355-60
2. JACC 2003;42:185-197
3. JACC 2004;43:2044-53
4. JAMA 2005;293:2634-40
5. N Engl J 2006; 354: 934-41

# Atrial Fibrillation Ablation

- CLASS 1 INDICATIONS:
  - Selected patients with symptomatic paroxysmal AF refractory or intolerant to at least one class I or III antiarrhythmic drug when a rhythm control strategy is desired
- CLASS III: Don't do it to get a patient off warfarin

# Atrioesophageal Fistula

- Presents 1-3 weeks AFTER ablation
  - Fever
  - TIA or other embolic phenomena
  - Chest pain
  - Odynophagia (but not necessarily)
  - Leukocytosis
  - Hematemesis (more rare)

# Atrioesophageal Fistula

- High mortality
- Get electrophysiology involved
- Get CT surgery involved
- Diagnose with CT with intravenous and water soluble contrast
- DO NOT DO EGD WITH INSUFLATION
- If test negative, may need to look again
- In some cases with high suspicion, take to OR directly even with negative tests



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**A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS  
WITH ATRIAL FIBRILLATION**

THE ATRIAL FIBRILLATION FOLLOW-UP INVESTIGATION OF RHYTHM MANAGEMENT (AFFIRM) INVESTIGATORS\*

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The New England Journal of Medicine

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**A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS  
WITH RECURRENT PERSISTENT ATRIAL FIBRILLATION**

ISABELLE C. VAN GELDER, M.D., VINCENT E. HAGENS, M.D., HANS A. BOSKER, M.D., J. HERRE KINGMA, M.D.,  
OTTO KAMP, M.D., TSJERK KINGMA, M.Sc., SALAH A. SAID, M.D., JULIUS I. DARMANATA, M.D.,  
ALPHONS J.M. TIMMERMANS, M.D., JAN G.P. TIJSSEN, Ph.D., AND HARRY J.G.M. CRIJNS, M.D.,  
FOR THE RATE CONTROL VERSUS ELECTRICAL CARDIOVERSION FOR PERSISTENT ATRIAL FIBRILLATION STUDY GROUP\*

STAF (n=200)- no difference in composite endpoint of death and thromboembolic events

PIAF (n=252)- No difference in symptomatic improvement

HOT CAFÉ (n=205)- No difference in composite death, thromboembolic events, hemorrhage



# Why ever consider rhythm control?

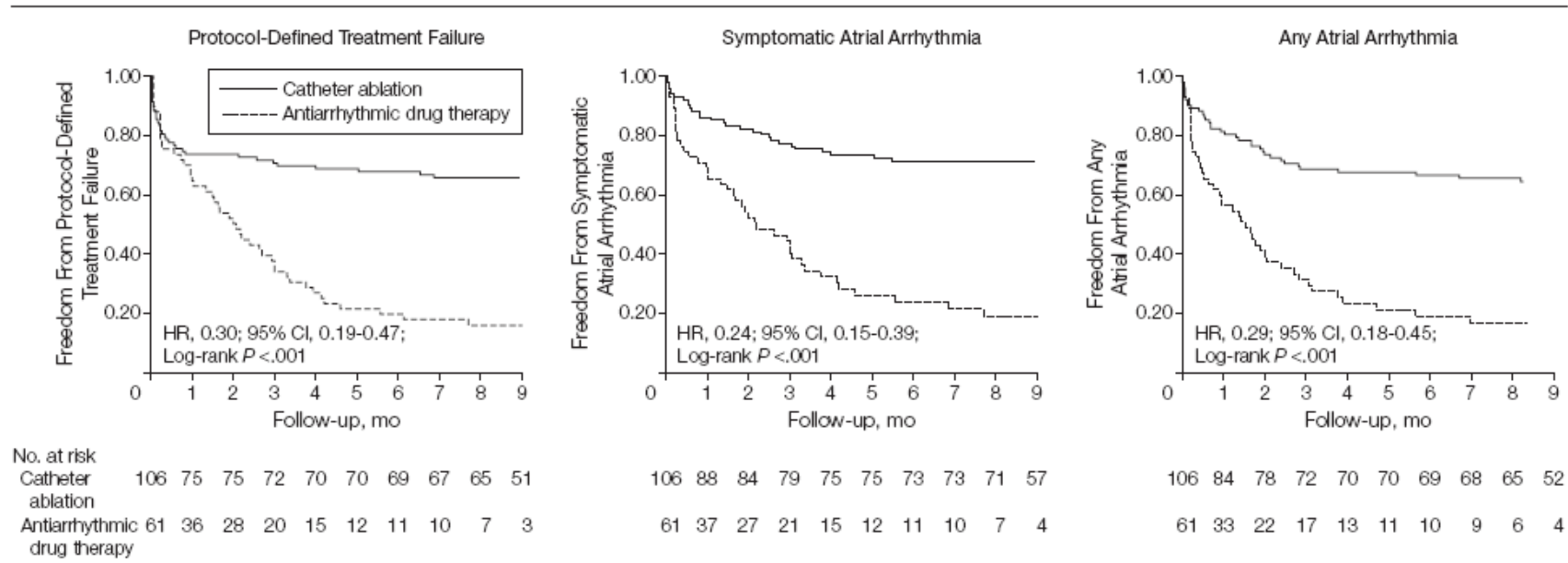
- Unlikely to include symptomatic patients in those studies
  - Rationale for rhythm control is primarily symptoms
  - Sometimes rationale is to help rate control
- Warfarin was stopped when sinus apparent
- Antiarrhythmic drugs don't work very well
- Evidence that those in sinus lived longer

# Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation

## A Randomized Controlled Trial

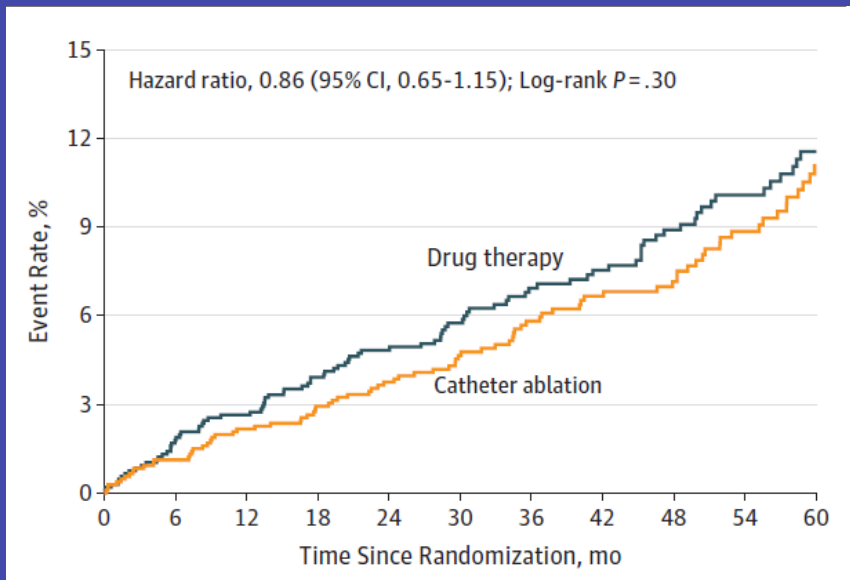
JAMA. 2010;303(4):333-340

**Figure 2.** Kaplan-Meier Curves of Time to Protocol-Defined Treatment Failure, Recurrence of Symptomatic Atrial Arrhythmia, and Recurrence of Any Atrial Arrhythmia by Treatment Group

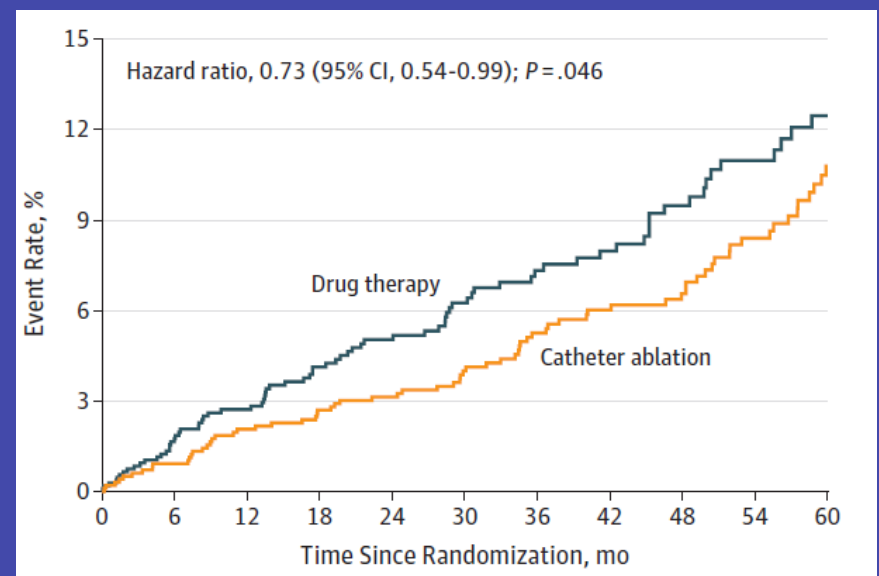


# Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation

## The CABANA Randomized Clinical Trial



Intention to treat



Per protocol

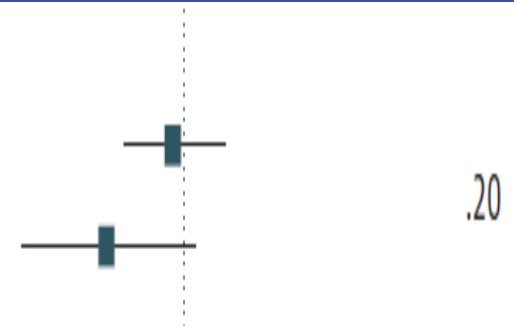
9.2% cross-over ablation → medicine  
27.5% cross-over medicine → ablation

# 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

History of congestive heart failure

No	68/934 (3506)	72/931 (3500)	0.95 (0.68-1.32)
Yes	21/174 (650)	29/163 (547)	0.61 (0.35-1.08)



.20

Intention to treat

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

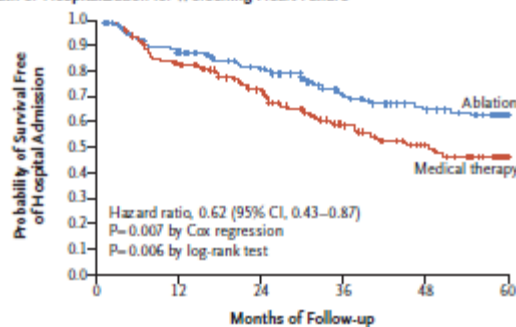
FEBRUARY 1, 2018

VOL. 378 NO. 5

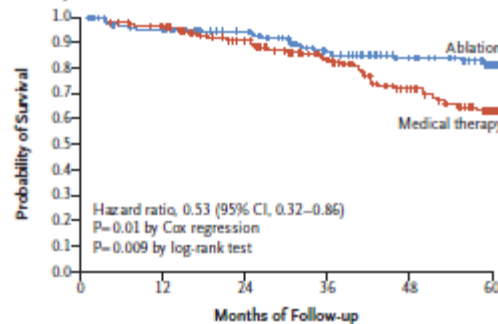
## Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators\*

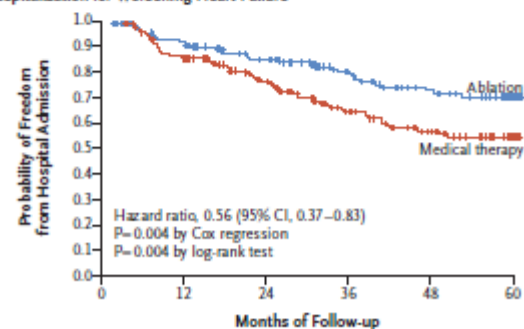
**A** Death or Hospitalization for Worsening Heart Failure



**B** Death from Any Cause



**C** Hospitalization for Worsening Heart Failure



# Conclusions

- Work-up consists of a good history, echo and basic labs
- There is no one best way to achieve rate control
- Stroke prophylaxis must always be considered
  - NOACs (or DOACS) are now first line
- A rhythm control strategy remains a reasonable option to help with symptoms

# Thank You

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Join the  Health eHeart™

The logo for Health eHeart features a stylized heart shape composed of several overlapping circles in shades of red, orange, and green.

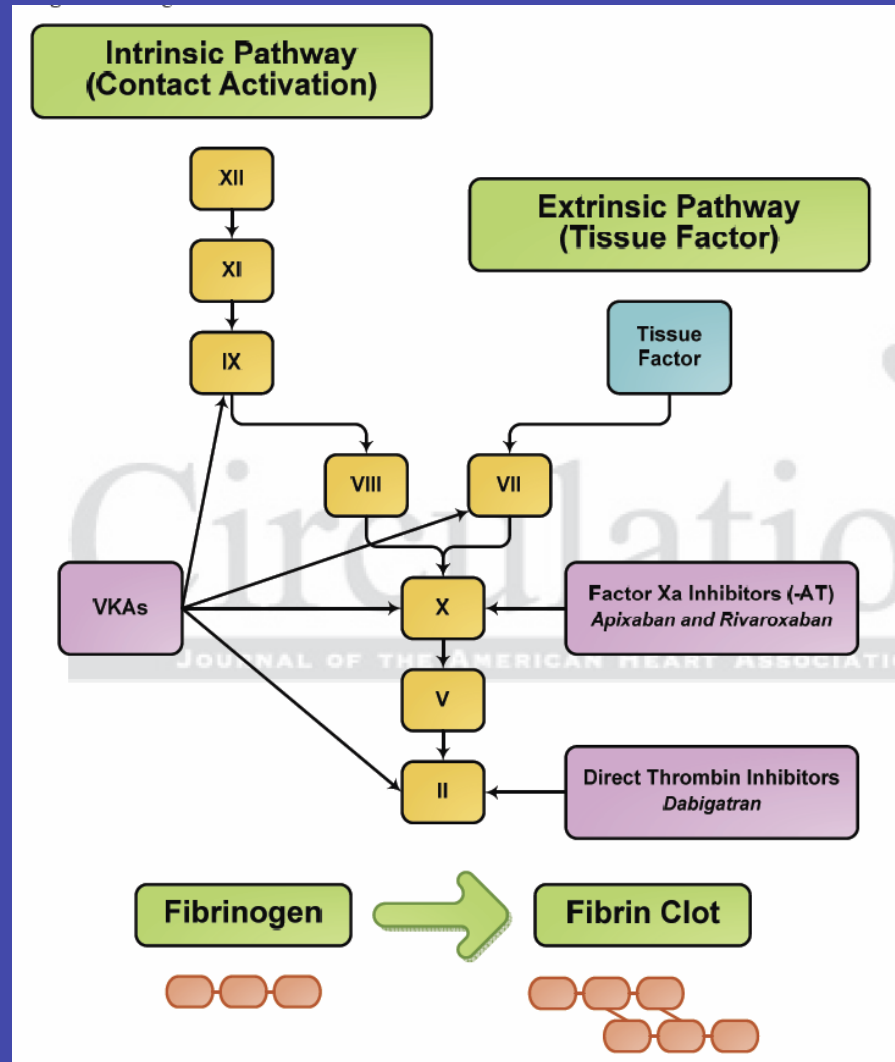
Study <https://www.health-eheartstudy.org/>

<b>Drug</b>	<b>Dose reduction</b>	<b>Other idiosyncracies</b>
Dabigatran=Pradaxa	CrCl 15-30 ml/min	Dyspepsia ~11% (acid core)
Rivaroxaban=Xarelto	CrCl 15-50 ml/min	pK maybe really 2x day drug
Apixiban=Eliquis	2 out of 3: Creatinine > 1.5, age >80, weight <60 kg	Might be used in hemodialysis
Edoxaban=Savaysa	CrCl 15-50 ml/min	Contraindicated if CrCl > 95 ml/min Drug interactions (verapamil and dronaderone increases)



# Novel Anticoagulants

- Reversibility?



## Reversal of Rivaroxaban and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects

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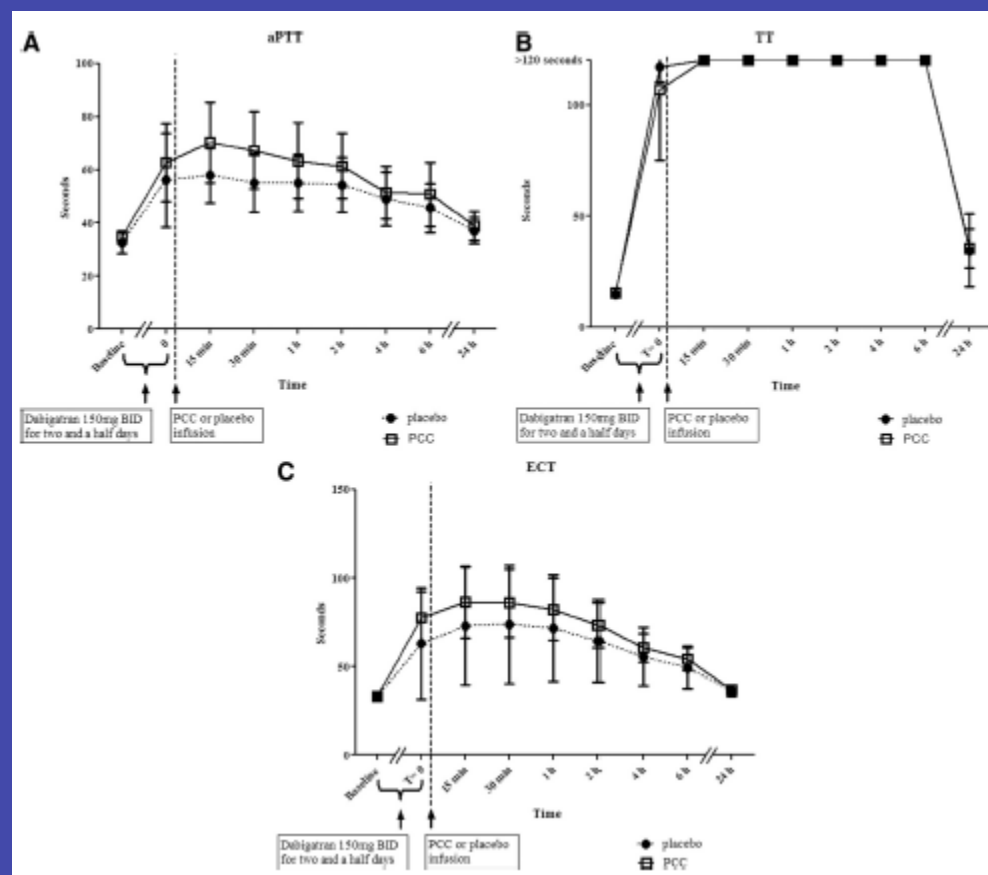
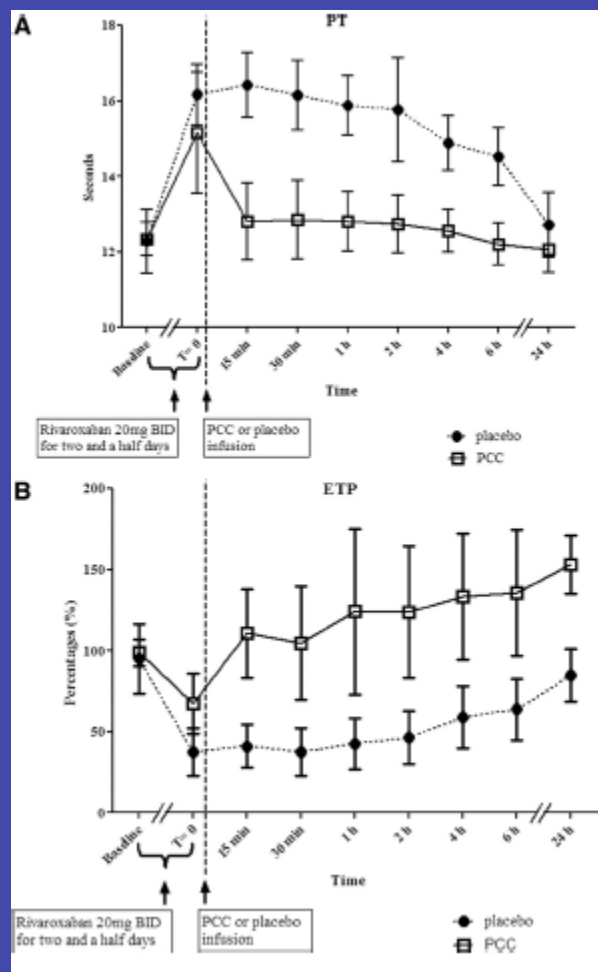


Figure 2. Effect of dabigatran followed by prothrombin complex concentrate (PCC) or placebo on the adjusted partial thromboplastin

ORIGINAL ARTICLE

## Idarucizumab for Dabigatran Reversal

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- Announcement of FDA approval 10/16/15