Management of Atrial Fibrillation in the Hospitalized Patient

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Disclosures

Research:
• NIH
• PCORI
• SentreHeart
• Gilead
• 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
• It is expected to affect > 4 million by 2030
• Affects ~4% of everyone over age 60 and ~10% of everyone over age 80
• The age-adjusted incidence is increasing

1. Miyasaka Y. Circulation 2006;114:119-125
My patient has AF
What work-up do I need to do?

- 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\(^1\)
- 15% of all strokes in the US can be attributed to AF\(^1\)
- AF is associated with an increase in mortality, from 1.3-2 times\(^2\)


Atrial Fibrillation and Other Bad Things

- AF increases risk of:
  - Heart failure\(^1\)
  - Dementia\(^2\)

Atrial Fibrillation and Other Bad Things

Incident Atrial Fibrillation and Risk of End-Stage Renal Disease in Adults With Chronic Kidney Disease
Nihal Bansal, Dongjie Fan, Chi-yeun Hsu, Juan D. Ortóñez, 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

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
</tr>
<tr>
<td>Adjusted for patient characteristics, cardiovascular risk factors, and medication use*</td>
</tr>
<tr>
<td>1.18 (1.06–1.31)</td>
</tr>
<tr>
<td>1.67 (1.46–1.91)</td>
</tr>
</tbody>
</table>

Atrial Fibrillation and Other Bad Things

Original Investigation

Atrial Fibrillation and the Risk of Myocardial Infarction

Fehdan Z. Sollman, MD, MD, NS; Monika M. Delfino, MD; Paul Muntner, PhD; Halina Holevska, MD, PhD; Farah Z. Dawood, MD; Nal A. Zakai, MD; Evan L. Thacker, PhD; Suzanne Judd, PhD; Virginia J. Howard, PhD; George Howard, DHSc, David M. Harrington, MD, MHS; Mary Cushman, MD, MSc

*JAMA Internal Medicine* Published online November 4, 2013
Among Cryptogenic Stroke Patients, AF can be found in:

- 0-3%
- 3-10%
- 10-20%
- 20-30%
Among Cryptogenic Stroke Patients, AF can be found in:

1. 0-3%
2. 3-10%
3. 10-20%
4. 20-30%

- 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%)¹
  – Strokes on warfarin are significantly less severe²
  – Warfarin reduced overall mortality in AF patients³

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%)\(^1\)

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

<table>
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<tr>
<th>Trial</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>994, 1,032, 1,068, and 3,200</td>
</tr>
<tr>
<td>2.</td>
<td>4,540, 4,895, 5,352, and 6,105</td>
</tr>
<tr>
<td>3.</td>
<td>7,511, 7,965, 9,003, and 9,423</td>
</tr>
<tr>
<td>4.</td>
<td>10,055, 12,607, 12,934, and 13,544</td>
</tr>
<tr>
<td>5.</td>
<td>14,264, 18,113, 18,201, and 21,105</td>
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</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>20%</td>
</tr>
<tr>
<td>2.</td>
<td>20%</td>
</tr>
<tr>
<td>3.</td>
<td>20%</td>
</tr>
<tr>
<td>4.</td>
<td>20%</td>
</tr>
<tr>
<td>5.</td>
<td>20%</td>
</tr>
</tbody>
</table>
VERSUS WARFARIN IN RANDOMIZED TRIALS OF AF PATIENTS

<table>
<thead>
<tr>
<th>Drug</th>
<th>What it blocks</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran=Pradaxa</td>
<td>Thrombin</td>
<td>Twice a day</td>
</tr>
<tr>
<td>Rivaroxaban=Xarelto</td>
<td>10a</td>
<td>Once a day</td>
</tr>
<tr>
<td>Apixiban=Eliquis</td>
<td>10a</td>
<td>Twice a day</td>
</tr>
<tr>
<td>Edoxaban=Savaysa</td>
<td>10a</td>
<td>Once a day</td>
</tr>
</tbody>
</table>
### VERSUS WARFARIN in AF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preventing Stroke or Thromboembolism</th>
<th>Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran=Pradaxa</td>
<td>Better</td>
<td>Similar</td>
</tr>
<tr>
<td>Rivaroxaban=Xarelto</td>
<td>Similar</td>
<td>Similar</td>
</tr>
<tr>
<td>Apixiban=Eliquis</td>
<td>Better</td>
<td>Better</td>
</tr>
<tr>
<td>Edoxaban=Savaysa</td>
<td>Similar to better</td>
<td>Better</td>
</tr>
</tbody>
</table>

### VERSUS WARFARIN in AF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Intracranial bleeding</th>
<th>GI Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran=Pradaxa</td>
<td>Much less</td>
<td>More</td>
</tr>
<tr>
<td>Rivaroxaban=Xarelto</td>
<td>Much less</td>
<td>More</td>
</tr>
<tr>
<td>Apixiban=Eliquis</td>
<td>Much less</td>
<td>Similar</td>
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<td>More</td>
</tr>
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### Novel Anticoagulants

- **Reversibility?**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose reduction</th>
<th>Other idiosyncracies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran=Pradaxa</td>
<td>CrCl 15-30 ml/min</td>
<td>Dyspepsia ~11% (acid core)</td>
</tr>
<tr>
<td>Rivaroxaban=Xarelto</td>
<td>CrCl 15-50 ml/min</td>
<td>pK maybe really 2x day drug</td>
</tr>
<tr>
<td>Apixiban=Eliquis</td>
<td>2 out of 3: Creatinine &gt; 1.5, age &gt;80, weight &lt;60 kg</td>
<td>Might be used in hemodialysis</td>
</tr>
<tr>
<td>Edoxaban=Savaysa</td>
<td>CrCl 15-50 ml/min</td>
<td>Contraindicated if CrCl &gt; 95 ml/min Drug interactions (verapamil and dronaderone increases)</td>
</tr>
</tbody>
</table>
Reversal of Rivaroxaban and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects
Elise S. Eerenberg, Pieter W. Kamphuisen, Meertien K. Sjøklint, Joost C. Meijers, Harry R. Boer and Marcel Levis

Circulation, 2011;124:1573-1579; originally published online September 6, 2011;

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Idarucizumab for Dabigatran Reversal
Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.

Announcement of FDA approval 10/16/15
• “Real world”
• Dabigatran v warfarin
• Danish Registry
• Propensity matched
• N= >12,000

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%
The Watchman Device in 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\textsuperscript{1}

\textit{Fountain RB \textit{et al.} Am Heart J 2006}

Lariat made by SentreHeart

- No randomized outcomes data
- May be considered if cannot anticoagulate
• FIRST POINT CLASS 1: Antithrombotic therapy should be individualized based on shared decision making
• Recommend using CHA$_2$DS$_2$-VASc
• Oral anticoagulation for CHA$_2$DS$_2$-VASc $\geq$ 2
• Anticoagulation options for nonvalvular AF include warfarin, dabigatran, rivaroxaban, or apixaban

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation
Anticoagulation

• For patients with nonvalvular AF unable maintain INRs, any of the novel anticoagulants are recommended

• **WHADYA MEAN NONVALVULAR AF?**
  • AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair
    – CLASS III (Harm): dabigatran should not be used with AF in patients with a mechanical heart valve

Anticoagulation

• For patients with nonvalvular AF and a CHA$_2$DS$_2$-VASc of 0, it is reasonable to omit *antithrombotic* therapy

• What about CHA$_2$DS$_2$-VASc of 1? → See FIRST POINT ABOVE
  – CLASS 2B: no antithrombotic or an anticoagulant or aspirin may be considered

• Be careful about renal function if prescribing novel drugs
Bridging
Bridging

• OK to just start warfarin (or the new agents) without heparin
• On warfarin:
  – Low risk: can hold for a week
  – High risk (mechanical valve, prior stroke, higher CHA₂DS₂-VASc) can consider unfractionated or low molecular weight heparin
  – Continue (as is done in many EP procedures)

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

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

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation
“Let’s just cardiovert back to sinus rhythm so we don’t need to worry about anticoagulation.”

I decide to go with

- Most thrombi in atrial fibrillation arise from the left atrial appendage
- 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: 1, 2
  – 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: 1, 2
  – 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%),\textsuperscript{1-5}
  - Atrial fibrillation ablation, based primarily on pulmonary vein isolation
- A great option for symptomatic patients
- An ELECTIVE PROCEDURE

2. JACC 2003;42:185-197
3. JACC 2004;43:2044-53
4. JAMA 2005;293:2634-40
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

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
  - Theoretical benefits in the young
- Warfarin was stopped when sinus apparent

Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation: A Randomized Controlled Trial

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
Conclusions

• Work-up consists of a good history, echo and basic labs

• There is no one best way to achieve rate control
  – Trial and error
  – Patients go fast outside the hospital all the time

• Stroke prophylaxis must always be considered
  – The options tailored to the individual patient

• A rhythm control strategy remains a reasonable option to help with symptoms

Thank You