WHO AM I?

Family Physician

Faculty

TMH Family Medicine Residency
WHO ARE YOU?

Audience Participation

Are you in:

A. Retail Pharmacy
B. Hospital Pharmacy
C. Other Outpatient Pharmacy
D. Student
E. Other
I do not have (nor does any immediate family member have) a vested interest in or affiliation with any corporate organization offering financial support or grant money for this continuing education program, or any affiliation with an organization whose philosophy could potentially bias my presentation.
DISCLOSURES

- It is the postprandial “witching hour”

- Only covering AFib in the hemodynamically stable patient

- Based on 2014 guidelines – not exhaustive

- You are not the envy of my 7 y/o listening to me for 90 min
OBJECTIVES

Pharmacist

- Know how to use CHA₂DS₂-VASc to estimate risk of thromboembolism in Afib
- Know how to use HAS-BLED to estimate risk of significant bleeding in Afib
- Know advantages and disadvantages of rate control vs. rhythm control in Afib
- Understand the advantages and disadvantages of anti-platelet agents vs. anticoagulants for stroke reduction in AFib.

Pharmacy Technician

- Understand the pathophysiology of Atrial Fibrillation
- Identify advantages and disadvantages of rate control vs. rhythm control in managing AFib
- Recognize the advantages and disadvantages of anti-platelet agents vs. anticoagulants for stroke reduction in AFib.
Why Should You Care?

Atrial Fibrillation:
- Common Problem
- Geriatric Problem – primarily
- Risky
- Costly
- Multiple Pharmacologic Therapies
- Frequent Drug-Drug Interactions

Fun Stats:\(^1:\)
- Prevalence
  - ~ 3 – 6 million cases
  - 9% of population 66+
  - 2% of population < 66
- 760,000 Hospitalizations/yr
- Contributes to 130,000 deaths/yr
- Costs $6 Billion/yr
NORMAL CARDIAC PHYSIOLOGY

Sinus Rhythm

- Diastole (cardiac filling)
- Systole
  - SA node firing
  - Atrial depolarization/contraction
  - AV Nodal pause → conduction
  - Conduction via His-Purkinje system
  - Ventricular depolarization
- Diastole

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg
PATHOPHYSIOLOGY OF AFIB

Atrial Fibrillation

- Systole
  - Disorganized atrial firing
  - “Fibrillation” of atria
  - Erratic AV nodal conduction
  - Erratic ventricular contraction

- Irregular diastole

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg
Irregular Tachyarrhythmia

- Uncoordinated depolarization of cardiac atria leading to:
  - Loss of atrial function
  - Irregular ventricular contraction
  - Inconsistent ventricular filling
  - Decreased cardiac output

- Absence of consistent P-waves on EKG

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg
ETIOLOGY

- Largely unknown\textsuperscript{2}
- Inflammation
- Fibrosis
- Structural & Electrical Remodeling
- Further Remodeling
- Cardiovascular Disease
- Ectopic foci/reentrant pathways
PATHOLOGY FROM ATRIAL FIBRILLATION

Atrial Pooling

Atrial/LAA Thrombus

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.png

PATHOLOGY FROM ATRIAL FIBRILLATION

Atrial Fibrillation

Sinus Rhythm

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg
Embolic Stroke

Morbidity
RISK FACTORS

General
- Age
- Sex
- DM
- HTN
- OSA
- Obesity
- Hyperthyroidism

Cardiac
- Past MI
- CHF
- Valvular dz
- s/p CT surgery - 20-60%
CLINICAL PRESENTATIONS

- Asymptomatic
- Palpitations
- Fatigue
- Dyspnea
- Presyncope/syncope
- Angina
- Acute pulmonary edema
- Stroke/TIA

https://images.medicinenet.com/images/appictures/heart-attack-signs-s1-facts.jpg
DIAGNOSING ATRIAL FIBRILLATION

- Irregular Pulse – Palpation
- Irregular rhythm – Auscultation
- 12 – Lead EKG

http://accessmedicine.mhmedical.com/data/books/hurs13/hurs13_c0408001.gif
Immediately after diagnosis of atrial fibrillation in a patient who is hemodynamically stable, first consideration should be given to:

A. Restoring normal sinus rhythm
B. Controlling the heart rate to less than 100
C. Anticoagulation to reduce risk of thromboembolism
D. Ruling out associated ischemia
E. MRI scan of the brain to rule out associated stroke
TREATING ATRIAL FIBRILLATION
TREATING ATRIAL FIBRILLATION

Diagnosis ➔ ↓ Risk Thromboembolism ≈ Stroke Prevention
THROMBOEMBOLIC RISK REDUCTION

- Thromboembolism
- Embolic Stroke
- Severe Bleeding
- Hemorrhagic Stroke

- AP
- DAP
- Anticoagulation
THROMBOEMBOLIC RISK REDUCTION

- Antiplatelet Therapy
  - ASA

- Dual Antiplatelet Therapy (DAPT)
  - ASA + P2Y12 Inhibitors

- Anticoagulation
  - Vitamin K Antagonist (VKA) – warfarin
  - Direct Oral Anticoagulants (DOAC)

- Left Atrial Appendage Occlusion
**THROMBOEMBOLIC RISK REDUCTION**

**Antiplatelet vs. No Therapy**

- No Benefit Reducing
  - Systemic Emboli
  - Mortality
- Modest Reduction Ischemic Stroke
- Modest Increase Hemorrhagic Stroke
- Benefits ≈ Harms for AFib Alone

**Conclusion**

- Mono AP Tx ≈ No Tx
- ASA monotherapy only in very low risk situations (CHA$_2$DS$_2$-VASc =1)
- P2Y12 Inhibitors alone not recommended as alternative
THROMBOEMBOLIC RISK REDUCTION

DAP vs. Mono-AP³

- Decreased risk of ischemic stroke
- No impact on:
  - All Cause Mortality
  - Systemic Emboli
  - Hemorrhagic Stroke
- Increased risk major bleeding

Conclusion

- DAP Tx > Mono-AP Tx³
THROMBOEMBOLIC RISK REDUCTION

Anticoagulation vs No Tx/Mono-AP$^3$

- Decreased risk of ischemic stroke
- Decreased Mortality
- Decreased Systemic Emboli
- Increased major bleeding
- Increased hemorrhagic stroke

Conclusion$^{3,4}$

- Anticoagulation decreases TE in AFib
- Benefits > Harms (usually)
THROMBOEMBOLIC RISK REDUCTION

Anticoagulation vs. DAP$^3$

- Decreased risk of ischemic stroke
- Decreased Systemic Emboli
- No Difference in Mortality
- No Difference in Major bleeding
- Increase in Hemorrhagic Stroke

Conclusion$^{3,4}$

- Anticoagulation > DAP Tx
- Anticoagulation = 1$^{st}$ Line Tx
- Benefits > Harms…(usually)
THROMBOEMBOLIC RISK REDUCTION

**Warfarin+DAP vs. Warfarin+Mono-AP**
- Increased risk of ischemic stroke
- Increased All-Cause Mortality
- Increased Major Bleeding

**Conclusion**
- Warfarin+Mono-AP > Warfarin+DAP
- Oral Anticoagulant + Clopidogrel
- AFib in those w/ stents
THROMBOEMBOLIC RISK REDUCTION

Dual Antiplatelet Therapy

ASA
+
?Agent

Conclusion

- No recommendation in guidelines

- Clopidogrel most common
THROMBOEMBOLIC RISK REDUCTION

- Oral Anticoagulants – Which is best in AFib?

  - Warfarin – Vitamin K antagonist
  - Apixaban – anti-Xa
  - Rivaroxiban – anti-Xa
  - Dabigatran – anti-thrombin
**THROMBOEMBOLIC RISK REDUCTION**

**Warfarin vs. DOAC**

- Warfarin
- vs
- Apixaban
- Dabigatran
- Rivaroxaban

**Conclusion**

- Generally comparable
- Consider reduced dose DOAC in mod-severe renal dz
- Do not use in ESRD
- DOACs should be considered within their FDA licensed indications
# THROMBOEMBOLIC RISK REDUCTION

<table>
<thead>
<tr>
<th></th>
<th>Apixaban</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>≥ 76</td>
<td>≥ 76</td>
<td>≥ 76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 66 w/ DM, CAD, HTN</td>
<td></td>
</tr>
<tr>
<td><strong>History</strong></td>
<td>Prior Stroke or TIA</td>
<td>Prior Stroke, TIA or systemic embolism</td>
<td>Prior Stroke or TIA</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td>DM, HTN, Symptomatic CHF</td>
<td>CHF w/ EF &lt; 40%, NYHA Class ≥ 2</td>
<td>DM, HTN, CHF</td>
</tr>
</tbody>
</table>
ANTICOAGULATION

Personalized Risk/Benefit Analysis

Clotting Risk

CHA$_2$DS$_2$-VASc

Bleeding Risk

HAS-BLED
THROMBOEMBOLIC RISK: $\text{CHA}_2\text{DS}_2\text{-VASC}$

$\text{CHA}_2\text{DS}_2\text{-VASC}^5$

- Published in 2010
- Score correlated to TE risk
- Low risk are very low risk - may not require anticoagulation
- Tool recommended by 2014 guidelines

- CHF/LV dysfunction
- Hypertension
- Age $\geq 66$
- Age $\geq 76$
- Diabetes mellitus
- Sex – Female
- Stroke/TIA/Thromboembolism
- Vascular Disease (MI, PAD, Aortic plaque)
BLEEDING RISK: HAS-BLED

HAS-BLED<sup>6</sup>

- Published 2010

- Validated estimation tool

- 1 year risk major bleed
  - 2 g/dL ↓ Hgb
  - Transfusion

- Recommended by 2014 guidelines

- HTN
- Age > 66
- Abnormal Renal Fx
- Abnormal Liver Fx
- Stroke/TIA/VTE
- Bleeding - H/o Major Event
- Labile INR
- Excess Alcohol
- Drugs - antiplatelet/NSAIDs
BLEEDING RISK: MODIFIABLE

HAS-BLED

- HTN
- Labile INR
- Excess" Alcohol
- Drugs - antiplatelet/NSAIDs
- Age > 66
- Abnormal Renal Fx
- Abnormal Liver Fx
- Stroke/TIA/VTE
- Bleeding - H/o Major Event

CHA$_2$DS$_2$-VASc

- Hypertension
- CHF/LV dysfunction
- Age $\geq$ 66
- Age $\geq$ 76
- Diabetes mellitus
- Sex – Female
- Stroke/TIA/Thromboembolism
- Vascular Disease (MI, PAD, Aortic plaque)
THROMBOEMBOLIC RISK REDUCTION

- Anticoagulation
- DAP
- AP

Severe Bleeding
Hemorrhagic Stroke

Thromboembolism
Embolic Stroke
CASE - JOAN

Joan is a 76 y/o female with history of HTN and DM presents to the office of her PCP for routine follow-up. Vital sign measurement shows a weight of 176 lbs. Blood pressure is 138/78, and she is found to have an irregular pulse at a rate of 80. She reports feeling normal. EKG confirms recent labs showed a serum creatinine of 1.2 and was otherwise normal.

1. Estimate her risk of stroke in the next year.

2. Recommend therapy to reduce her risk of stroke. Estimate risk of stroke and bleeding on this regimen.
CASE - JOAN

- Age – 76
- Female
- HTN
- Diabetes
- Wt 176
- Scr 1.2

- [http://www.acc.org/anticoagevaluator](http://www.acc.org/anticoagevaluator)
**Case - Joan**

<table>
<thead>
<tr>
<th></th>
<th>No Tx</th>
<th>DAPT</th>
<th>Warfarin</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE Risk</td>
<td>6.7%</td>
<td>5.6%</td>
<td>3.3%</td>
<td>2.6%</td>
</tr>
<tr>
<td>NNT</td>
<td>23</td>
<td>15</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Bleed Risk</td>
<td>0.6%</td>
<td>3.8%</td>
<td>9.4</td>
<td>6.5%</td>
</tr>
<tr>
<td>NNH</td>
<td>31</td>
<td>11</td>
<td>17</td>
<td></td>
</tr>
</tbody>
</table>

**CHA$_2$DS$_2$-VASc = 5**

**HAS-BLED = 4**
THROMBOEMBOLIC RISK REDUCTION

What if Anticoagulation:

- Contraindicated
- Failed

Left Atrial Appendage Occlusion

Conclusions

1. Benefits of anticoagulation outweigh risks for most people
2. Do not withhold anticoagulation solely due to fall risk.
3. Agent choice based on clinical features and patient preference

### THROMBOEMBOLIC RISK REDUCTION

<table>
<thead>
<tr>
<th>CHA₂DS²-VASc</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No Intervention</td>
</tr>
<tr>
<td>1</td>
<td>Consider ASA vs No Tx</td>
</tr>
<tr>
<td>2+</td>
<td>Anticoagulation – Take bleeding risk into account</td>
</tr>
</tbody>
</table>

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4. Conclusions
QUESTION:

In someone diagnosed with atrial fibrillation, treating to maintain sinus rhythm (rhythm control) compared to treating to control heart rate (rate control)?

A. Reliably improves symptoms
B. Protects against thromboembolism
C. Improves mortality
D. All of the above
E. None of the above
TREATING ATRIAL FIBRILLATION

Diagnosis → Stroke Prevention → Rate Control → Consider Rhythm Control
RATE VS RHYTHM: ADVANTAGES

Rate Control

- Preserves Diastolic Filling Time
- Avoid Effects of RVR…(usually)
  - Palpitations
  - Dyspnea
  - Presyncope/syncope
  - Angina
  - Acute pulmonary edema
- Medications Safe
- Less Complicated

Rhythm Control

- Preserve Atrial Synchrony
- Preserve Cardiac output
- Avoid Effects of RVR…(usually)
RATE VS RHYTHM: DISADVANTAGES

Rate Control
- Accept Atrial dyssynchrony
- Anticoagulation Need
- Breakthrough RVR
- Symptoms Not Always Resolved

Rhythm Control
- Complex
- Medication Side Effects
- Medication Interactions
- Anticoagulation Still Needed
- Recurrent AFib
- Rate Control Through Process
RATE > RHYTHM... (EXCEPT)

- New Onset
- Reversible Cause
- CHF thought due to AFib
- Rhythm Control More Suitable

- Failure to control rate
- Symptoms Despite Controlled Rate
RATE CONTROL

- ß-Blockers or Diltiazem
  - Digoxin – (if sedentary)
  - Combination Therapy
  - Rhythm Control
# Rate Control - Subpoints

<table>
<thead>
<tr>
<th>ß-Blockers</th>
<th>Non-dihydropyridine CCBs</th>
<th>Digoxin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typically Well Tolerated</td>
<td>Diltiazem &gt; Verapamil</td>
<td>Useful in CHF w/ ↓ EF</td>
</tr>
<tr>
<td>Not Sotalol</td>
<td>Avoid Verapamil + ß-Blockers³</td>
<td>Digoxin Toxicity</td>
</tr>
<tr>
<td></td>
<td>Avoid in CHF w/ ↓ EF</td>
<td></td>
</tr>
</tbody>
</table>
RATE CONTROL

Recommendations

- 1st line therapy - standard beta-blocker or rate-limiting calcium-channel blocker\(^3,4\)
- Consider symptoms, heart rate, comorbidities, patient preferences in choice\(^3,4\)
- Consider digoxin monotherapy only in sedentary patients with non-paroxysmal AFib\(^3\)
- Monotherapy failure – consider combination of any two\(^3\):
  - Beta-blocker
  - Diltiazem
  - digoxin
- Do not use amiodarone for long term rate control\(^2\)
RHYTHM CONTROL

Anticoagulation + Rate Control

Restoration of Sinus Rhythm

Maintenance of Sinus Rhythm
RHYTHM CONTROL

Atrial Fibrillation

Sinus Rhythm

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/images/AFib_heart.jpg
RHYTHM CONTROL

Embolic Stroke

Morbidity
RHYTHM CONTROL

Anticoagulation + Rate Control

Restoration of Sinus Rhythm

Maintenance of Sinus Rhythm
The preferred method for restoration of sinus rhythm in someone whose atrial fibrillation has persisted for > 48 hours, or is of unknown duration is:

A. Electrical cardioversion guided by transesophageal echocardiogram
B. Electrical cardioversion after 3 weeks of therapeutic INR on warfarin
C. Pharmacologic cardioversion with an antiarrhythmic agent
D. A and B
E. All of the above are equally acceptable
RHYTHM CONTROL

Restoration of Sinus Rhythm

- Electrical Cardioversion (EC)
- Pharmacologic Cardioversion
RHYTHM CONTROL

Electrical Cardioversion

- < 48 Hours
- > 48 Hours/Unknown

Anticoagulation

- Heparin
- LMWH
- DOAC
Rhythm Control

**Electrical Cardioversion**

- *< 48 Hours*
  - Anticoagulation
  - Transesophageal Echo Guidance
    - Anticoag ≥ 3 weeks before
- *> 48 Hours/ Unknown*
  - Anticoag ≥ 4 weeks after

**Anticoagulation**

- Heparin
- LMWH
- DOAC

**Anticoag ≥ 3 weeks before**

**Anticoag ≥ 4 weeks after**
RHYTHM CONTROL

Restoration of Sinus Rhythm
  - Electrical Cardioversion (EC)
  - Pharmacologic Cardioversion

- Class 1c Antiarrhythmics
  - Flecanide
  - Propafenone

- Class III Antiarrhythmics
  - Amiodarone
  - Dofetilide
RHYTHM CONTROL

Restored Sinus Rhythm

Maintenance of Sinus Rhythm
RHYTHM CONTROL

- Rhythm Maintenance
- Class 1c Antiarrhythmics
  - Flecanide
  - Propafenone
Rhythm Control

Rhythm Maintenance

Class 1c Antiarrhythmics

Class III Antiarrhythmics

Amiodarone

Sotalol

Dofetilide

Dronedarone
RHYTHM CONTROL

Rhythm Maintenance

Class 1c Antiarrhythmics
- Flecanide
- Propafenone

Class III Antiarrhythmics
- Amiodarone
- Sotalol
- Dofetilide
- Dronedarone
RESTORATION OF SINUS RHYTHM

Recommendations

- Electrical cardioversion 1st line – repeat if necessary

- AFib < 48 h – anticoagulation at time of EC and at least 4 weeks

- AFib > 48 h
  - Transesophageal guided cardioversion with anticoagulation before and at least 4 weeks
  - Warfarin x 3 weeks before and at least 4 weeks after

- Long-term anticoagulation after successful cardioversion based on CHA$_2$DS$_2$-VASc

- Pharmacologic Cardioversion – Flecanide, Propafenone, Dofetilide, Amiodarone
RHYTHM MAINTENANCE

Recommendations

- Amiodarone, Dofetilide, Dronedarone, Flecanide, Propafenone, Sotalol

- Avoid antiarrhythmics once AFib becomes permanent

- Consider amiodarone long term only if others have failed

- Do not use Class 1c antiarrhythmics if known ischemic or structural heart disease

- Dronedarone has several stipulations regarding its recommended use – not in CHF
Rhythm Control

Anticoagulation + Rate Control

Restoration of Sinus Rhythm

Maintenance of Sinus Rhythm
RHYTHM CONTROL

Anticoagulation + Rate Control

Restoration of Sinus Rhythm

< 48 Hours

Electrical Cardioversion

Anticoagulation

Heparin

LMWH

DOAC

> 48 Hours/Unknown

Transesophageal Echo Guidance

Anticoag x 3 weeks

Pharmacologic Cardioversion

Class 1c Antiarrhythmics

Flecainide

Propafenone

Amiodarone

Dofetilide

Dronedarone

Rhythm Maintenance

Class 1c Antiarrhythmics

Flecainide

Propafenone

Amiodarone

Sotalol

Dofetilide

Dronedarone

Class III Antiarrhythmics

Flecainide

Propafenone

Amiodarone

Sotalol

Suniti

Dofetilide

Dronedarone
RATE VS RHYTHM

Rate Control

- Anticoagulation
- β-Blockers or Diltiazem
- Digoxin – (if sedentary)
- Combination Therapy

Rhythm Control
RATE CONTROL

Atrial ablation

AV Nodal Ablation

http://anesthesiology.pubs.asahq.org/data/journals/JASA/930681/34F7F02.png

ATRIAL FIBRILLATION - SUMMARY

- Common source of risk & morbidity – especially in elderly

- Disorganized atrial depolarization → Atrial fibrillation → Atrial clot → Embolism

- Thromboembolism prevention → Anticoagulation > DAPT
  - Individualized risk estimation - CHA₂DS₂-VASc vs HAS-BLED

- Rate Control > Rhythm Control
  - Simplicity
  - Safety
  - No change in mortality
CASE: REVISITING JOAN

What to do?

- New diagnosis of AFib
- CHA$_2$DS$_2$-VASc - 5
- HAS-BLED – 4

Plan

- Discuss new diagnosis with associated risks.
- Begin DOAC
- Begin low-dose metoprolol to maintain rate
- Refer to Cardiologist for evaluation and planning of cardioversion
REFERENCES

QUESTIONS