21st CENTURY EPIDEMICS

- Obesity
- DM
- CHF
- Atrial fibrillation
Epidemiology of AF

- Most common sustained cardiac arrhythmia\(^1\)
- Currently affects 5.1 million Americans\(^2\)
- Prevalence expected to increase to 12.1 million by 2050 (15.9 million if increase in incidence continues)\(^2\)
- Preferentially affects men and the elderly\(^1,2\)
- Lifetime risk of developing AF: \(~1\) in 4 for adults \(\geq 40\) years of age\(^3\)

AF CONSEQUENCES

**Thromboembolism**
- Stroke: 4.5× increased risk
- Microemboli: reduced cognitive function
- Prothrombotic state

**Hospitalizations**
- Most common arrhythmia requiring hospitalization
- 2-3× increased risk for hospitalization

**Mortality**
- 2× increased risk independent of comorbid CV disease
- Sudden death in HF and HCM

**Impaired Hemodynamics**
- Loss of atrial kick
- Irregular ventricular contractions
- HF
- Tachycardia-induced cardiomyopathy

**Reduced QoL**
- Palpitations, dyspnea, fatigue, reduced exercise tolerance

- AF is an enormous contributor to the growing cost of medical care

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Progression: AF Begets AF

Paroxysmal
Self-terminating AF episodes

Persistent
Sinus can be restored electrically or chemically

Permanent
Sinus cannot be maintained

Atrial remodeling
"AF begets AF"

Trigger initiation

Substrate maintenance

Heart Rhythm Disorders
GOALS OF THERAPY

1. Control rate to prevent cardiomyopathy
   - Resting < 80 bpm
   - Moderate activity < 110 bpm

2. Relieve symptoms
   - Rhythm vs rate control

3. Reduce risk of thromboembolism
   - Anticoagulation
   - Left atrial appendage closure
MYTH

1. CAD is the most common cause
Acute infarcts: transient AF in 5-10% usually associated with CHF
Chronic CAD: rare cause unless CHF
CARDIAC ETIOLOGY

• HTN
• Valvular heart disease (mitral)
• CHF
• Cardiomyopathy
• Pericarditis
• Congenital heart disease
• CAD
NON CARDIAC ETIOLOGY

- Sleep apnea
- Obesity
- Diabetes
- Alcohol: risk increases 7%/daily drink
- AGE
- Familial
- Lung disease, PE
- Hyperthyroidism < 5%
- Infections, illness, post operative
- Caffeine?
# AF Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF</td>
<td>4.5-6</td>
</tr>
<tr>
<td>Valve Disease</td>
<td>2-3.5</td>
</tr>
<tr>
<td>Age</td>
<td>2.1</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>2.1</td>
</tr>
<tr>
<td>HTN</td>
<td>1.5</td>
</tr>
<tr>
<td>DM</td>
<td>1.5</td>
</tr>
<tr>
<td>Male</td>
<td>1.5</td>
</tr>
<tr>
<td>CAD</td>
<td>1.4</td>
</tr>
</tbody>
</table>
2. Syncope is common with AF due to a rapid ventricular response
Atrial Fibrillation

Sinus arrest

Junctional escape

Sinus rhythm
3. You cannot have AF if you have a pacemaker
PACEMAKER IN AF

Atrial rate
300-600 bpm

Ventricular rate
100-175 bpm
CASE 1

74 year old man with hx HTN, HFpEF c/o 1-2 weeks of DOE and fatigue.

BNP 247
What do you do next?

A. Lasix
B. Metoprolol
C. TTE
D. Stress echo
E. Anticoagulate and cardiovert
ATRIAL FLUTTER
ATRIAL FLUTTER

• Saw tooth pattern in II, III, AVF loss of the isoelectric baseline
• Flutter waves in V1 look like sinus p waves
• Flutter rate usually 300 bpm
• Ventricular rate often 150 from 2:1 block (range 130-170)
  – 3:1 rate 100
  – 4:1 rate 75
  – Irregular rate if variable block
ATRIAL FLUTTER

Atrial flutter circuit

Ectopic beats (triggers)
ATRIAL FLUTTER ABLATION

Ablation line made by catheter to ‘cut’ the circuit and cure atrial flutter
COARSE ATRIAL FIBRILLATION

ECG tracing showing coarse atrial fibrillation in leads I, II, III, aVR, aVL, aVF, V1, V2, V3, V4, V5, and V6.
CASE 2

52 yr old healthy man with mild-moderate obesity and HTN

- Annual follow up visit has irregular pulse 120-130. ECG confirms atrial fibrillation.

What do you do next?
• Labs: CBC, BMR, Mg, TSH
• Echocardiogram
• Holter monitor
• Identify triggers: ETOH, sleep apnea
• Start beta blocker
• Evaluate need for anticoagulation
• Rate control vs rhythm control
HOSPITALIZATION/URGENT CV

• Decompensated CHF
• Acute MI
• Hypotension
• Intolerable symptoms
• Palpitations
• Dizziness/LH
• Fatigue/malaise
• Dyspnea
• Exercise intolerance
• Chest pain
• Can be asymptomatic
## CHADS2 VASc: STROKE RISK

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>CHADS2 VASc Score</th>
<th>Annual Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure</td>
<td>+1 point</td>
<td>~0%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>+1 point</td>
<td>1.3%</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>+2 point</td>
<td>2.2%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+1 point</td>
<td>3.2%</td>
</tr>
<tr>
<td>Stroke/TIA History</td>
<td>+2 point</td>
<td>4.0%</td>
</tr>
<tr>
<td>Vascular Disease</td>
<td>+1 point</td>
<td>6.7%</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>+1 point</td>
<td>9.8%</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>+1 point</td>
<td>9.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15.2%</td>
</tr>
<tr>
<td>CHA\textsubscript{2}DS\textsubscript{2}–VASc Score</td>
<td>Recommendation</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>No therapy is reasonable</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>OAC, aspirin, or no therapy may be considered</td>
<td></td>
</tr>
<tr>
<td>≥2 or prior stroke/TIA</td>
<td>OAC recommended</td>
<td></td>
</tr>
<tr>
<td>≥2 and ESRD (CrCl &lt;15 mL/min) or hemodialysis</td>
<td>Warfarin (INR 2.0-3.0) is reasonable</td>
<td></td>
</tr>
</tbody>
</table>
## DOAC PHARMAKOKINETICS

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxiban</th>
<th>Apixiban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>Thrombin</td>
<td>FXa</td>
<td>FXa</td>
</tr>
<tr>
<td><strong>Peak levels</strong></td>
<td>1-2hrs</td>
<td>2-4hrs</td>
<td>3-4hrs</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>hepatic</td>
<td>CYP 3A4</td>
<td>CYP 3A4</td>
</tr>
<tr>
<td><strong>Renal excretion</strong></td>
<td>80%</td>
<td>33%</td>
<td>25%</td>
</tr>
<tr>
<td><strong>Half life</strong></td>
<td>12-18hrs</td>
<td>5-13hrs</td>
<td>12-15hrs</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>BID</td>
<td>Daily</td>
<td>BID</td>
</tr>
<tr>
<td><strong>Antidote</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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All NOACs; Stroke or Systemic Embolic Events

RE-LY (Pradaxa®)
(150 mg)
Risk Ratio (95% CI)
0.66 (0.53-0.82)

ROCKET AF
(Xarelto®)

ARISTOTLE
(Eliquis®)

ENGAGE AF-TIMI 48
(Lixiana®)
(60 mg)
Risk Ratio (95% CI)
0.80 (0.67-0.95)
0.88 (0.75-1.03)
0.88 (0.75-1.02)

Combined
(Random effects model)
Risk Ratio (95% CI)
0.81 (0.73-0.91)
P < .0001

N = 58,541

Heterogeneity P = .13

Favors NOAC
Favors Warfarin

Secondary Efficacy Outcome

Risk Ratio (95% CI)

- Ischemic Stroke: $0.92 (0.83-1.02)$, $P = .10$
- Hemorrhagic Stroke: $0.49 (0.38-0.64)$, $P < .0001$
- MI: $0.97 (0.78-1.20)$, $P = .77$
- All-cause Mortality: $0.90 (0.85-0.95)$, $P = .0003$

Heterogeneity $P = NS$ for all outcomes

Favors NOAC  Favors Warfarin

All NOACs: Major Bleeding

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk Ratio (95% CI)</th>
<th>N = 58,498</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY (150 mg)</td>
<td>0.94 (0.82-1.07)</td>
<td></td>
</tr>
<tr>
<td>ROCKET AF</td>
<td>1.03 (0.90-1.18)</td>
<td></td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td>0.71 (0.61-0.81)</td>
<td></td>
</tr>
<tr>
<td>ENGAGE AF-TIMI 48 (60 mg)</td>
<td>0.80 (0.71-0.90)</td>
<td></td>
</tr>
<tr>
<td>Combined (Random effects model)</td>
<td>0.86 (0.73-1.00)</td>
<td>P = .06</td>
</tr>
</tbody>
</table>

Heterogeneity P = .001

Major GI Bleeding in Studies of NOACs

Incidence of Major GI Bleeding, %/year

- **Apixaban**: NOAC = 0.76, Warfarin = 0.86
- **Dabigatran 110**: NOAC = 1.12, Warfarin = 1.02
- **Edoxaban 30**: NOAC = 1.23, Warfarin = 1.02
- **Dabigatran 150**: NOAC = 1.51, Warfarin = 1.02
- **Edoxaban 60**: NOAC = 1.51, Warfarin = 1.23
- **Rivaroxaban**: NOAC = 1.24

**P-values and HRs**
- **Apixaban**: P = 0.43, RR = 1.10 (0.86, 1.41)
- **Dabigatran 110**: P = 0.37, HR = 0.67 (0.53, 0.83)
- **Edoxaban 30**: P < 0.001, RR = 1.50 (1.19, 1.89)
- **Dabigatran 150**: P < 0.001, RR = 1.23 (1.02, 1.50)
- **Edoxaban 60**: P = NR, HR = 1.61 (1.30, 1.99)

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NOAC CONTRAINDICATIONS

• Valvular atrial fibrillation
  • Mechanical heart valve
  • Moderate – severe rheumatic mitral stenosis

• Drug-drug interactions

• Renal insufficiency?
  • Not studied GFR < 30ml/min
  • FDA labelling GFR > 15ml/min
  • Apixaban < 15 ml/min
Primary Endpoint: All-Cause Mortality

Mortality (%)

Rhythm
Rate

p = 0.058

Time (Years)

Rhythm N: 2033 1932 1807 1316 780 255
Rate N: 2027 1925 1825 1328 774 236
TREATMENT

• Anticoagulate with NOAC 3-4 weeks
• DC cardioversion anticoagulate 1 mo
• Consider beta blocker or diltiazem/verapamil
• Sleep study
• Exercise and weight loss
CASE 3

62 year old man with PAF CV 1 year ago, frequent episodes palpitations associated with fatigue, SOB, dizziness lasting 12-24 hrs.

Holter monitor confirms PAF

Meds: Toprol XL 50 mg, Mg

Echo: Normal EF/valves
Mild LAE
The next best step is

A. Increase metoprolol to 50 bid
B. Change metoprolol to diltiazem
C. Start flecainide or propafenone
D. Start amiodarone
E. AF ablation
## Rhythm control

### Antiarrhythmic drugs for AF

#### Efficacy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sinus rhythm after 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>25%</td>
</tr>
<tr>
<td>Class IA*, IC*, Sotalol</td>
<td>40-60%</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>60-70%</td>
</tr>
</tbody>
</table>

*Concurrent use of AV nodal blocking drug
FAVORABLE FOR ABLATION

- Younger < 70
- Paroxysmal rather than persistent
- Symptomatic
- Failed an antiarrhythmic drug
- Structurally normal heart
ATRIAL FIBRILLATION ABLATION

• Success rate
  • Paroxysmal 70-80%
  • Persistent 50-60%

• Complication rate 4%
  • Vascular access most common
  • Pericardial tamponade 1%

• Antiarrhythmic Rx stopped after 3 mo
• Anticoagulate for 2-3 months long term is based on CHADS2 VASc score
CASE 4

- 78 yr old man paroxysmal now persistent atrial fibrillation over the last 6 months. Symptomatic with fatigue, dyspnea, palpitations
- Medications: metoprolol 100 bid, asa
- Pulse 115 irregular, no CHF
- Echo EF 40% severe biatrial enlargement, moderate MR/TR
The best treatment option is?

A. Add digoxin
B. Add diltiazem
C. Cardioversion
D. AF ablation
E. AV node ablation and pacemaker (ablate and pace)
AVN ABLATION/PACEMAKER

- Regular ventricular rate without need for AVN blocking agents
- Improve LV function
- Improve QOL
- Pacer dependent
- Atrium still in atrial fibrillation
Anticoagulate based on CHADS 2 VASc score
LEADLESS PACEMAKER
CASE 5

- 76 year old female with a history of PAF, HTN, CAD, ETOH abuse.
- Mechanical fall with subarachnoid and subdural hematoma on warfarin.
- TIA 1 month after anticoagulation stopped.
- CHADS2VASC 7; 11% stroke risk/yr.
- HASBLED 5: Major bleed rate 9.1%.
• Device alternative to anticoagulation
• CHADS2VASc ≥ 3, poor candidate for long term anticoagulation (GIB, ICH, high risk lifestyle/occupation)
RESULTS

<table>
<thead>
<tr>
<th>Event</th>
<th>HR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All stroke or SE</td>
<td>1.02</td>
<td>0.94</td>
</tr>
<tr>
<td>Ischemic stroke or SE</td>
<td>1.95</td>
<td>0.05</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0.22</td>
<td>0.004</td>
</tr>
<tr>
<td>Ischemic stroke or SE &gt;7 days</td>
<td>1.56</td>
<td>0.21</td>
</tr>
<tr>
<td>CV/unexplained death</td>
<td>0.48</td>
<td>0.006</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.73</td>
<td>0.07</td>
</tr>
<tr>
<td>Major bleed, all</td>
<td>1.00</td>
<td>0.98</td>
</tr>
<tr>
<td>Major bleeding, non procedure-related</td>
<td>0.51</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Favors Watchman: 0.01 - 1  
Favors warfarin: 1 - 10  
Hazard Ratio (95% CI)
COMPLICATIONS

- Clinical Trial Experience
- Post-Approval Experience

<table>
<thead>
<tr>
<th>Procedural Parameters</th>
<th>Aggregate Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Procedures</td>
<td>6,720</td>
</tr>
<tr>
<td>Implantation Success, %</td>
<td>94.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complication Rates</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial Tamponade</td>
<td>1.24%</td>
</tr>
<tr>
<td>Procedure-Related Stroke</td>
<td>0.18%</td>
</tr>
<tr>
<td>Device Embolization</td>
<td>0.25%</td>
</tr>
<tr>
<td>Procedure-Related Death</td>
<td>0.06%</td>
</tr>
</tbody>
</table>
Implant – 45 day
Warfarin: dosage to achieve INR 2.0-3.0
Aspirin: 81 mg while on warfarin
Clopidogrel: No

LAA Seal per 45 Day TEE

45 day – 6 Months
Warfarin: No
Aspirin: 325 mg*
Clopidogrel: Yes

6 Months – 5 Years
Warfarin: No
Aspirin: 325 mg*
Clopidogrel: No

45 day – 6 Months*
Warfarin: Yes
Aspirin: 81 mg while on warfarin
Clopidogrel: No

6 Months – 5 Years
Warfarin: Discontinued when seal is adequate
Aspirin:
On warfarin - 81 mg
Off warfarin - 325 mg* indefinitely
Clopidogrel: No