Atrial Fibrillation & Anticoagulation

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Objectives

• Understand that older adults suffer more adverse events from atrial fibrillation but also gain more benefit from anticoagulation.
• Describe the risks and benefits of various anticoagulation options.
• Manage anticoagulation challenges.

What is A-fib?

• Irregularly irregular heartbeat
• No p-waves
• SA node does not initiate the heartbeat
• The atrium does not contract but quivers
• Blood does not get pumped to the ventricle
What’s the big deal?

What's the big deal?

Weakness from decreased cardiac output

![Cardiac output graph]

What can we do about it?

- Rhythm control with medications did not improve survival
  Talajic et al. 2010 JACC 55(17):1796–802
- Ablation of pulmonary vein, SA or AV node did not reduce stroke
  – Heat or freezing

What’s the big deal?

What’s the big deal?

Fast heart beat decreased cardiac output

![Cardiac output graph]
Tachycardia

- Exercise prescription:
  - (220-age) x 85%
- Treat fast heartbeat, tachycardia aggressively in older adults with medications
  - Beta blocker
  - Calcium Channel blocker
  - Rarely digoxin

Prevalence of A-fib

Risk Factors

- Age >60
- Obesity
- Diabetes
- Hypertension
- Coronary artery disease
- Sleep apnea
- Excessive alcohol or stimulant use

Heart Rhythm Society 2016
Contributing Factors

- Enlarged atrium
  - Mostly due to high blood pressure
  - Valve leakage from sclerosis
- Sinoatrial (SA) node atrophies much faster
  - At age 80 only 10% of SA node cells are left

Preventing A-fib

- Diet:
  - Low in: salt, saturated fats, meat
  - High in: nuts, legumes, fruits vegetables
- Blood pressure control
- Stop smoking
- Weight loss
- Exercise

Treatment of Sleep Apnea Prevents Atrial Fibrillation

- 698 CPAP users and 549 non-CPAP users.
- Patients treated with CPAP had a 42% decreased risk of AF (pooled risk ratio, 0.58; 95% CI, 0.47 - 0.70; p <0.001)
- Most benefit in young, male, obese

Qureshi WT, et al. 2015 Am J Cardiol. 50002-0149(15)01930-x PMID: 26482182
What’s the big deal?

• Stagnant blood in the atrium will clot
• Broken off pieces of blood clot, emboli, will block blood from getting to brain tissue
• The brain area beyond the clot will die from lack of oxygen
• The dead brain tissue cannot control the body’s function
• Resulting in a stroke

Left Hemiparesis

• Left sided neglect difficult to rehabilitate
• Patients do not realize that the left is their hand, leg, etc.

Right Hemiparesis

• Most R hemiparesis associated with speech impairment, aphasia
• Expressive aphasia always associated with various levels of receptive aphasia
  – Cannot rely on patient understanding
Aspirin Stroke Prevention

• Aspirin
  – No differences in outcomes between different doses of aspirin (SOR A)
• Aspirin plus clopidogrel (Plavix)
  – Does not reduce the risk of secondary stroke compared to aspirin alone
  – Significantly increases the risk of life-threatening bleeding (SOR A)
• Warfarin no better than aspirin therapy for secondary stroke prevention, without A-fib
  http://www.cochrane.org/reviews/en/ab000187.html

A-Fib Stroke Prevention

• High risk of stroke
  – Atrial fibrillation
    • Anticoagulants (warfarin) reduce the risk of stroke in A-fib
    • Antiplatelet therapy (Aspirin)
      – Contraindication to anticoagulation
      – Not as effective as anticoagulants

A-fib Stroke Prevention

• Aspirin reduces stroke by 21%
• Warfarin reduces stroke 64%
• This differences increases the older we get.
  Van Walraven, et al. 2009 Stroke 40;1410-6
**CHA₂DS₂-VASc**

- CHF
- HTN
- Age ≥ 75 (2pts)
- Diabetes
- Prior Stroke, TIA, PE (2pts)
- Vascular disease
- Age 65-74
- Sex (female)

<table>
<thead>
<tr>
<th>CHA₂DS₂-VASc Score</th>
<th>Stroke Risk %</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
</tr>
<tr>
<td>5</td>
<td>6.7</td>
</tr>
<tr>
<td>6</td>
<td>9.8</td>
</tr>
<tr>
<td>7</td>
<td>9.6</td>
</tr>
<tr>
<td>8</td>
<td>6.7</td>
</tr>
</tbody>
</table>

**Inadequate Anticoagulation**

- 148,000 patients in Adelaide, Australia
- 318 strokes in 301 patients in 12 months
- Fatality rate for 1st stroke 19%
- 84% ischemic stroke
  - 42% Cardioembolic
  - 36% A-fib
- 85% inadequately anticoagulated

Leyden JM, et al. 2013 Stroke. 44(5):1226-31

**Inadequate Anticoagulation**

146 NH residents w A-fib, avg. age 88.4
51% Aspirin, 28% warfarin, 21% none.
All should have been anticoagulated, based on CHA₂DS₂-VASc ≥2.
7% should have received Aspirin based on HEMORR²HAGES ≥4.

Nishtala, et al. 2016 Clin Pharm Ther
HEMORR2HAGES Score for Major Bleeding Risk

- Hepatic or Renal disease: 1 point
- Alcohol Abuse: 1 point
- Age ≥75: 1 point
- Low platelet count of function: 1 pt
- Past bleeding: 2 points
- HTN uncontrolled: 1 point
- Anemia <13 ♂ <12 ♀: 1 point
- Genetics CYP 2C9: 1 point
- Fall risk: 1 point
- Stroke History: 1 point

0-1 low risk
2-3 intermed.
≥4 high risk for bleed

HAS-BLED Score for Major Bleeding Risk

- HTN (BP>160)
- Kidney disease
- Liver disease
- Stroke history
- Alcohol history
- Labile INR
- Major bleeding or predisposition
- Age ≥65
- Meds predisposing to bleeding (NSAID,....)


ATRIA Score for Major Bleeding Risk

- Anemia <13 ♂ <12 ♀: 3 points
- Renal function <30 ml/min: 3 points
- Age ≥75: 2 points
- Prior intracranial, GI bleed:1 point
- HTN: 1 point

Fang 2011 J Am Coll Cardiol 58: 395-401
Go 2001 JAMA 285:2370-2375
Bleeding Risk Models not in very Elderly with A-fib

1157 patients ≥80 yo on warfarin
Followed over 3 years for bleeding

<table>
<thead>
<tr>
<th>Model / Statistic</th>
<th>ROC major bleed</th>
<th>Factors in multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAS-BLED</td>
<td>0.57</td>
<td>prior bleed, NSAIDs, ASA</td>
</tr>
<tr>
<td>ATRIA</td>
<td>0.58</td>
<td>anemia</td>
</tr>
<tr>
<td>HEMORRHAGES</td>
<td>0.57</td>
<td>anemia, low platelet count, Fx</td>
</tr>
<tr>
<td>Study 1157 pts x3y</td>
<td>NNT 22, NNH 91</td>
<td>anemia, antiplatelet therapy</td>
</tr>
</tbody>
</table>


Atrial Fibrillation-Stroke Prevention

- INR below 2.0 is not effective for stroke prevention
- INR above 3.0 considerably raises the risk of hemorrhage (SOR A)
- Do not stop warfarin for dental surgery
  - Wang 1998 Arch Int Med 158: 1610-6
- It takes 295 falls per year to outweigh the benefits of warfarin in A-fib
  - Man-Son-Hing 1999 Ann Int Med 159; 677-85

Warfarin Risk - Benefit

Bleeding Risk  All Event Risk

Fang 2006 J Am Ger Soc 54;1231-4
Warfarin after GI Bleed

- Patients with GI bleed on warfarin
- Resuming warfarin
  - lower risk for death (HR, 0.31; 95% CI, 0.15-0.62)
  - Higher rebleed risk if resumed in 1-7 days, no difference after 7 days,
  - No deaths from rebleed
  Witt 2012 Arch In Med

SAMe-TT2R2 score

<table>
<thead>
<tr>
<th>Condition/influencing factor</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female)</td>
<td>1</td>
</tr>
<tr>
<td>Age (&lt;60 years)</td>
<td>1</td>
</tr>
<tr>
<td>Medical history (two of the following: hypertension, diabetes, MI, PAD, congestive heart failure, history of stroke, pulmonary disease, hepatic or renal disease)</td>
<td>1</td>
</tr>
<tr>
<td>Treatment (interacting medications e.g. amiodarone)</td>
<td>1</td>
</tr>
<tr>
<td>Tobacco use (within 2 years)</td>
<td>2</td>
</tr>
<tr>
<td>Race (non-Caucasian)</td>
<td>2</td>
</tr>
</tbody>
</table>

Score 0-2 <65% time in therapeutic INR range (TTR)
Score >2 Education on INR control or Novel Oral Anticoagulants

Palaneti 2016 Thromb Haemost. 28;115(6)

Difficult to Control INR

- Know your time in therapeutic range:
  - 2016 UW Health 79%
- Medication changes
- Diet
- Brand name Coumadin
- Adding vitamin K to attenuate fluctuations
Self Monitoring and Mgmt

28 randomized trials w 8950 participants
– Self-management ↓ all-cause mortality (RR 0.55, 95% CI 0.36 to 0.84; n= 3058; studies = 8); self monitoring did not.
– ↓ thromboembolic events (RR 0.58, 95% CI 0.45 to 0.75; n= 7594; studies = 18;
– Low to moderate quality evidence, bias

Heneghan, et al. 2016 Cochrane CD003839. PMID: 27378324

Medications

Medications Lower INR

Carbamazepine Cholestyramine Dicloxacillin
Griseofulvin Mercaptopurine Mesalamine Nafcillin
Phenobarbital Phenytoin Primidone Ribavirin Rifabutin
Rifampin Sucralfate

Herbals or Supplements
Vitamin K Coenzyme Q10 Ginseng St. John's wort Green tea Alalfa Angelica Arnica Chamomile Echinacea
Ginseng Melilot Saw palmetto Sweet woodruff Tonka beans

Medications raise INR

Acetaminophen Alcohol (binge) Allopurinol Amiodarone
Argatroban Aspirin Azithromycin Bactrim Chlortal hydrate
Chloramphenicol Cimetidine Ciprofloxacin Citalopram
Clarithromycin Clofibrate Dantrolen Diltiazem Disulfiram
Disopyramide Doxycycline Entacapone Erythromycin
Felbamate Fenofibrate Fluconazole Fluouracil Fluvoxamine
Gemfibrozil Influenza vaccine Isoniazid Itraconazole
Levofoxacin Metronidazole Miconazole Moxalactam Neomycin Norfloxacin Ofloxacin Omeprazole Phenylbutazone
Piroxicam Propafenone Propranolol Quinidine Ritonavir
Sertraline Simvastatin Sulfinpyrazone Sulfamethoxazole
Tamoxifen Testosterone Tetracycline Vitamin E Voriconazole
Zafirlukast
Herbals Raise INR
Anise Asafoetida Chamomile Clove Danshen Devil’s claw Dong quai Fenugreek Feverfew Fish oil Garlic Ginger Ginkgo Grapefruit Horse chestnut Licorice root Mango Meadowsweet Onion Papain Quassia Red clover Rue Clover Tumeric Willow bark Vitamin E

Foods that affect INR
Eat the same amount of the same food every week
- Greens
- Carrots
- Green beans
- Beans
- Soy
- Oils
- Meat, esp organ meat
- Grapefruit
- Cranberries
- Alcohol
- Anything ....

Brand name Coumadin
- 40,000 patients were switched repeatedly between brand name and generic warfarin (crossover trial)
  - No statistical significant difference in INR
  - In individual patients some had variations in levels
  - Worth a try

Add Vitamin K

• 80 patients, age 45-79
• 100 µg vitamin K tablets
• INR between 2-3 ↑ from 32% to 57%
• Cost $4 for 100 pills
• Consider ↑ to 200 µg vitamin K


Add Vitamin K

150 mcg Vitamin K vs. placebo 6 months
• More attentive monitoring of warfarin therapy improved time in the therapeutic range in both Vitamin K and placebo groups
• Vitamin K reduced extreme INR variation


Novel Oral Anticoagulants

• Rivaroxaban (Xarelto)
• Apixaban (Eliquis)
• Dabigatran (Pradaxa)

• Each costs about $400 a month
Novel Oral Anticoagulants

- Increased risk of GI bleed
- Not reversible
- Dabigatran on Beers list, high bleed risk, cleared by the kidney
- Comparison with warfarin at 62%-65% in the therapeutic range INR 2-3

A-fib and Cancer

- 34,691 women ≥45 years free of AF, cardiovascular disease and cancer at baseline were followed 1993-2013 within the Women’s Health Study
  - First 3 months after new-onset AF 3 fold risk of cancer (HR, 3.54; 95% CI, 2.05-6.10; P < .001)
  - 1 yr after AF onset 42% increased risk (adjusted HR, 1.42; 95% CI, 1.18-1.71; P < .001)
  - New-onset cancer, the relative risk of AF was increased the first 3 months (HR, 4.67; 95% CI, 2.85-7.64; P < .001) but not thereafter

Conen 2016 JAMA Cardiol 1(4):389-396
Summary

• Best evidence for stroke prevention is in Atrial fibrillation with warfarin (stay tuned for other anticoagulants)
• The oldest old benefit the most from anticoagulation in A-fib
• No need to stop anticoagulation for falls or minor surgeries