THE PROJECT HAS A 70% CHANCE OF MINOR SUCCESS AND A 30% CHANCE OF CORPORATE RUINATION.

I LIKE THOSE ODDS. WHEN CAN WE START?

START?

I WISH WE HAD TEN MORE PROJECTS LIKE THIS ONE.
Atrial Fibrillation

David Stultz, MD
Cardiology Fellow, PGY 6
November 2, 2005
Patient Presentation

• A 76 year old male with history of hypertension and hyperlipidemia presents for routine examination. You detect an irregular pulse and heart rate. An EKG confirms atrial fibrillation with a heart rate of 85.

• New Diagnosis of Atrial Fibrillation
  – What tests?
  – What medications?
Atrial Fibrillation

- Most common sustained arrhythmia
- Estimated 2.3 million patients in the United States
- Incidence of 3.8% in patients >60 years
- Incidence of 9% is patients >80 years
- Increases relative risk of death 1.3-2x
Relative risk of Stroke and Death with Atrial Fibrillation

Figure 3. Relative risk of stroke and mortality in patients with AF compared with patients without AF. Source data are from the Framingham Heart Study (11), Regional Heart Study (8), Whitehall study (8), and Manitoba study (18).
## CONDITIONS RELATED TO ATRIAL FIBRILLATION

<table>
<thead>
<tr>
<th>Cardiac causes</th>
<th>Noncardiac causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive heart disease</td>
<td>Autonomically mediated (sympathetic or parasympathetic)</td>
</tr>
<tr>
<td>Valvular disease</td>
<td>Toxin exposure</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>Endocrinopathy (especially thyroid disease)</td>
</tr>
<tr>
<td>Cardiomyopathy (all forms)</td>
<td>Pulmonary disease</td>
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<tr>
<td>Pericardial disease</td>
<td>Neurologic disorders</td>
</tr>
<tr>
<td>Intracardiac masses</td>
<td>Idiopathic</td>
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<tr>
<td>Electrical disease</td>
<td></td>
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<tr>
<td>Sinus node dysfunction</td>
<td></td>
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<tr>
<td>Tachycardia-induced</td>
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<tr>
<td>Familial</td>
<td></td>
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<tr>
<td>Cardiothoracic surgery</td>
<td></td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td></td>
</tr>
</tbody>
</table>
Etiology - Hypertensive

- Hypertensive heart disease
  - Accounts for about 50% of cases in developed countries
  - May be due to LA dilatation secondary to decreased LV compliance
  - Associated CAD
Etiology - Valvular

• Valvular Heart Disease
  – Mitral stenosis due to rheumatic disease
  – Increased stroke risk – 20% of patients with AF and MS will have embolic event
  – Stroke risk 3-7x that of sinus rhythm with MS
  – AF is infrequent with isolated Aortic stenosis
Etiology - Surgery

- Cardiac Surgery
  - Common complication of cardiac surgery
  - 20-40% incidence following CABG, often postoperative days 2-8
  - Risk of AF following surgery
    - Elderly
    - Prior AF
    - Right coronary artery stenosis
    - Beta blockers discontinued preoperatively
Etiology - Other

• Thyroid disease
  – Occurs in 20-25% of elderly with thyrotoxicosis
  – About 1% of new onset AF is due to hyperthyroidism
• Alcohol
  – Common cause of AF
  – Seen in up to 60% of binge drinkers
  – AF episodes coincide with heavy intake
• Cardiomyopathy
  – AF present in 28% of patients with hypertrophic cardiomyopathy
  – AF occurs in 20% of those with dilated cardiomyopathy
• Familial
  – Autosomal dominant – chromosome 10q22-q24

Crawford
Mechanism of Atrial Fibrillation

Multiple simultaneous re-entrant circuits

Rapid single circuit or focal source

Focal source

Pulmonary veins

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Sinus Rhythm vs. Atrial Fibrillation
Clinical Classification

- Acute – AF related to transient or reversible cause, or 1st episode of AF
- Chronic
  - Paroxysmal – self-terminating AF
  - Sustained
    - Persistent – AF that can be cardioverted
    - Permanent – AF that is resistant to cardioversion or inappropriate for cardioversion

Situational variants
- Vagal mediated – occurs at night or after meals
- Adrenergic mediated – AF during exercise, stress

Paroxysmal AF may become chronic
(8% at 1 year, 18% at 4 years)
NEWLY DISCOVERED AF

Paroxysmal

No therapy needed unless severe symptoms (e.g., hypotension, HF, angina pectoris)

Anticoagulation as needed

Persistent

Accept permanent AF

Anticoagulation and rate control as needed

Rate control and anticoagulation as needed

Consider antiarrhythmic drug therapy

Cardioversion

Long-term antiarrhythmic drug therapy unnecessary
Symptoms

- Asymptomatic – discovered by auscultation, pulse palpation, EKG, or Holter
- Major symptoms
  - Heart Failure
  - Angina
  - Hypotension
  - Presyncope
  - Syncope – usually with pre-excitiation, hypertrophic cardiomyopathy, or aortic stenosis
  - Stroke
  - Systemic Embolization
Symptoms

• Minor symptoms
  – Palpitations
  – Racing heart
  – Fatigue
  – Light-headedness
  – Increased urination
  – Shortness of breath
# Initial Evaluation

## Initial Evaluation of Patients with Atrial Fibrillation

### Minimum Evaluation
- History and physical exam
- ECG
- Chest X-ray
- Echocardiogram
- Laboratory studies – thyroid, renal function

### Optional Studies
- Exercise testing or ambulatory ECG
- Transesophageal echocardiogram
- Electrophysiologic study
History

- Symptoms
- Sustained or intermittent
- Complications
- Precipitating factors
- Relief of symptoms
- Duration/Frequency
- Prior treatment
Blood Tests

- Complete Blood Count
- Electrolytes
- Renal function
- Thyroid function
Chest X-ray

- May show congenital heart disease (ASD)
- Heart Size
- Presence of heart failure
- Coexisting intrathoracic pathology
EKG

- Rapid baseline oscillations
- Irregularly Irregular ventricular rate
- Absence of P waves
- ? Etiology
  - Left ventricular hypertrophy
  - Prior myocardial infarction
  - Pre-excitation
Atrial Fibrillation on EKG

http://www.ecglibrary.com/af_fast.html
Echocardiography

- Structural heart disease?
  - Valvular abnormalities
  - Congenital defects
  - Chamber size
    - Significant left atrial enlargement reduces success of cardioversion and long term maintenance of sinus rhythm. Also, LAE may increase risk of stroke
  - Pericardial thickening or effusion
  - Ventricular function
Electrophysiologic testing

• Limited role

• Possible indications
  – Atrial flutter or Supraventricular tachycardia is cause of atrial fibrillation
  – Other symptoms (pre-excitation, sinus node dysfunction, syncope) need clarification
  – Focal source amenable to ablation
Other studies

• Exercise stress testing
  – Anginal symptoms during episodic atrial fibrillation with rapid ventricular response or independent of atrial fibrillation
  – Assess for rate control during drug therapy

• Cardiac catheterization
  – Usually only indicated if symptoms or noninvasive tests suggest active ischemia
Pre-Management Assessment

• Are there any other associated arrhythmias or conduction abnormalities?
  – Pre-excitation
  – AV block
• Are there predisposing factors? Are they reversible or preventable?
• Is there a need for urgent intervention?
  – Hemodynamic instability
• Is there a need for rhythm control, or is rate control sufficient?
Acute Atrial Fibrillation Management

- Hemodynamic compromise – DC cardioversion
- Consider IV Heparin
- Rate control
  - Beta blockers
  - Calcium Channel Blockers
  - Digoxin
- Cardioversion if <48 hours duration
Paroxysmal Atrial Fibrillation Management

• Goals
  – Reduce frequency of paroxysms
  – Control rate during paroxysms
  – Prevent thromboembolism

• Digoxin may increase frequency and duration of paroxysms

• Calcium channel and Beta blockers may control ventricular rate, but not reduce frequency of attacks

• Antiarrhythmic therapy
  – Flecainide or propafenone considered in absence of structural heart disease
  – “Pill in the pocket” strategy
Pill in the Pocket

- 210 patients initially treated inpatient for recurrent atrial fibrillation
  - Excluded ischemic heart disease, valvular disease, dilated or hypertrophic cardiomyopathy
- Propafenone or flecainide used for inpatient treatment
- Mean followup 15 months
- 165 patients had 618 Afib episodes
- Prn propafenone or flecainide terminated 94% of Afib episodes
- 7% of patients had side effect, mostly nausea
- 1 patient had acceleration of rate → Atrial flutter with 1:1 conduction @210 bpm

Outcomes among 165 patients with at least one out-of-hospital drug-treated atrial fib recurrence

<table>
<thead>
<tr>
<th>End point</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of symptoms to drug ingestion, mean (min)</td>
<td>36</td>
</tr>
<tr>
<td>Palpitations stopped within 6 hours (%) of episodes</td>
<td>94</td>
</tr>
<tr>
<td>Time to symptom resolution after drug ingestion, mean (min)</td>
<td>113</td>
</tr>
<tr>
<td>Drug terminated all episodes within a patient (%)</td>
<td>84</td>
</tr>
<tr>
<td>Adverse drug effects developed at least once (%)</td>
<td>7</td>
</tr>
</tbody>
</table>

# Mean monthly events, 12 months prior vs follow-up period for 210 patients

<table>
<thead>
<tr>
<th>Event</th>
<th>Prior 12 months</th>
<th>During follow-up</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic atrial-fib episodes</td>
<td>59.8</td>
<td>54.5</td>
<td>NS</td>
</tr>
<tr>
<td>Calls for emergency-room atrial-fib intervention</td>
<td>45.6</td>
<td>4.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>15.0</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Chronic Atrial Fibrillation Management

• Underlying etiology?
• Rate control vs rhythm control
  – Heart rate 60-80 at rest, 90-115 during moderate exercise
• Thromboembolic prophylaxis
Risks for cardioversion failure and failure to maintain sinus rhythm

- Advanced age
- Duration of atrial fibrillation
  - Unlikely to maintain sinus rhythm when atrial fibrillation > 2 years duration
- Uncontrolled hypertension
- Severity of structural heart disease
  - Severe left atrial dilatation
- Other systemic diseases
Cardioversion

• Thromboembolism rare when AF duration is <48 hours
• When AF duration is >48 hours, thromboembolism occurs in 7% when no anticoagulation is used
• Most embolic events occur in 1st week after cardioversion
TEE before cardioversion

- Atrial fibrillation >48h or unknown
- Used to minimize duration of atrial fibrillation or reduce total anticoagulation time
- Evaluate for thrombus in the left atrial appendage
- If no thrombus, then may cardiovert followed by anticoagulation x 4 weeks
  - Risk of CVA 0.8% vs 0.5% for 3 weeks of prior coumadin
- If thrombus present, anticoagulation x 4 weeks then re-evaluate with TEE
Thrombus in left atrial appendage

TEE
Anticoagulation and Cardioversion

<table>
<thead>
<tr>
<th>Duration of arrhythmia</th>
<th>Anticoagulation before cardioversion</th>
<th>Anticoagulation after cardioversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;48 hours</td>
<td>Not required</td>
<td>Optional based on risk for recurrence</td>
</tr>
<tr>
<td>&gt;48 hours</td>
<td>Warfarin to achieve INR of 2–3 for 3 weeks, or</td>
<td>Warfarin to achieve INR of 2–3 for &gt;4 weeks</td>
</tr>
<tr>
<td></td>
<td>Transesophageal echo-cardiogram negative for thrombus</td>
<td>Heparin, then warfarin to achieve INR of 2–3 for &gt;4 weeks</td>
</tr>
</tbody>
</table>
Electrical Cardioversion

- Synchronized
- 200 J monophasic or 125J biphasic
- Ibutilide or other class III antiarrythmic may facilitate cardioversion
- Reports of intracardiac shock or transthoracic shock up to 720J used in refractory cases
Persistent Atrial Fibrillation
Difficult to maintain sinus rhythm

Arrhythmia-free survival after electrical cardioversion in patients with persistent atrial fibrillation. The lower curve represents outcome after a single shock when no prophylactic drug therapy was given. The upper curve depicts the outcome with repeated electrical cardioversions in conjunction with antiarrhythmic drug prophylaxis. ECV indicates electrical cardioversion; SR, sinus rhythm. Reproduced with permission from van Gelder et al., Arch Intern Med 1996;156:2585–92, © 1996, American Medical Association (110).
Nonembolic complications of electrical cardioversion

- Ventricular arrhythmia
- Sinus bradycardia
- Hypotension
- Pulmonary edema
- Skin burns
- Transient ST and T wave abnormalities
Torsades de Pointes
Following chemical cardioversion with ibutilide
Chemical cardioversion

- Many cases of new onset atrial fibrillation will spontaneously convert to sinus rhythm within 48 hours

<table>
<thead>
<tr>
<th>ANTIARRHYTHMIC DRUG DOSES FOR PHARMACOLOGICAL CARDIOVERSION AND PREVENTION OF ATRIAL FIBRILLATION RECURRENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>iv or oral therapy for rapid conversion</strong></td>
</tr>
<tr>
<td><strong>Class IA drugs</strong></td>
</tr>
<tr>
<td>Procainamide</td>
</tr>
<tr>
<td>Quinidine sulfate</td>
</tr>
<tr>
<td>Disopyramide</td>
</tr>
<tr>
<td><strong>Class IC drugs</strong></td>
</tr>
<tr>
<td>Flecainide</td>
</tr>
<tr>
<td>Propafenone</td>
</tr>
<tr>
<td><strong>Class III drugs</strong></td>
</tr>
<tr>
<td>Ibutilide</td>
</tr>
<tr>
<td>Sotalol</td>
</tr>
<tr>
<td>Amiodarone</td>
</tr>
<tr>
<td>Dofetilide</td>
</tr>
</tbody>
</table>
Antiarrhythmic therapy
Maintenance of sinus rhythm

• Amiodarone superior to sotalol and class I drugs
• Sotalol equivalent to class I drugs
• Propafenone may be drug of choice?
• Risk of proarrhythmia
  – Sinus node dysfunction or AV block
  – Class IA and III prolong QT interval
  – Class IA, IC, and amiodarone can cause atrial flutter; in absence of AV blockade may cause hemodynamic collapse with 1:1 conduction
### Table 3. Typical Doses of Drugs Used to Maintain Sinus Rhythm in Patients With Atrial Fibrillation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dosage</th>
<th>Potential Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone†</td>
<td>100–400 mg</td>
<td>Photosensitivity, pulmonary toxicity, polyneuropathy, GI upset, bradycardia, torsade de pointes (rare), hepatic toxicity, thyroid dysfunction</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>400–750 mg</td>
<td>Torsade de pointes, HF, glaucoma, urinary retention, dry mouth</td>
</tr>
<tr>
<td>Dofetilide‡</td>
<td>500–1000 mcg</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>Flecaïnide</td>
<td>200–300 mg</td>
<td>Ventricular tachycardia, congestive HF, enhanced AV nodal conduction (conversion to atrial flutter)</td>
</tr>
<tr>
<td>Procainamide</td>
<td>1000–4000 mg</td>
<td>Torsade de pointes, lupus-like syndrome, GI symptoms</td>
</tr>
<tr>
<td>Propafenone</td>
<td>450–900 mg</td>
<td>Ventricular tachycardia, congestive HF, enhanced AV nodal conduction (conversion to atrial flutter)</td>
</tr>
<tr>
<td>Quinidine</td>
<td>600–1500 mg</td>
<td>Torsade de pointes, GI upset, enhanced AV nodal conduction</td>
</tr>
<tr>
<td>Sotalol‡</td>
<td>240–320 mg</td>
<td>Torsade de pointes, congestive HF, bradycardia, exacerbation of chronic obstructive or bronchospastic lung disease</td>
</tr>
</tbody>
</table>

GI indicates gastrointestinal; AV, atrioventricular; and HF, heart failure.

*Drugs are listed alphabetically.

**The drugs and doses given here have been determined by consensus based on published studies.

†A loading dose of 600 mg per day is usually given for one month or 1000 mg per day over 1 week.

‡Dose should be adjusted for renal function and QT-interval response during in-hospital initiation phase.
Antiarrhythmic selection for persistent atrial fibrillation

Heart disease?

No (or minimal*)
- Flecainide
- Propafenone
- Sotalol
- Amiodarone, Dofetilide
- Disopyramide
- Procainamide
- Quinidine

Consider nonpharmacological options

Yes †

HF
- Amiodarone
- Dofetilide

CAD
- Sotalol
- Amiodarone
- Dofetilide

Hypertension
- LVH greater than or equal to 1.4 cm
  - Yes
  - Amiodarone
  - Disopyramide
  - Procainamide
  - Quinidine

  - No
  - Flecainide
  - Propafenone

- Amiodarone
- Dofetilide
- Sotalol
- Disopyramide
- Procainamide
- Quinidine

ACC 2001
Reducing Torsades de Pointes during antiarrythmic therapy

- **1C agents** (flecainide, propafenone)
  - QRS width should not exceed 150% of pretreatment width
  - Exercise testing useful to detect QRS changes at higher rates (use-dependence)

- **1A (procainamide, disopyramide, quinidine) and III (sotalol, dofetilide, *amiodarone)**
  - QTc should not exceed 520ms

- **Serial followup of renal function, electrolytes (K⁺ and Mg²⁺), and cardiac function**
Flecainide (IC) causing atrial flutter with 1:1 conduction
Rate Control

- **Digoxin**
  - Enhances vagal tone, prolongs AV nodal refractory period
  - Less effect during stress, fever, etc.
  - Onset of action several hours (even IV)
- **Beta Blockers**
  - Decrease resting heart rate and blunt HR response to exercise
  - May worsen vagally mediated atrial fibrillation
- **Calcium Channel Blockers**
  - Slow conduction in the AV node
  - Negative inotropes (especially verapamil)
## Medications for rate control

<table>
<thead>
<tr>
<th>DRUG LOADING AND MAINTENANCE REGIMENS FOR CONTROL OF VENTRICULAR RATE IN ATRIAL FIBRILLATION</th>
<th>Acute intravenous therapy</th>
<th>Chronic oral therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>2.5–5mg every 5 minutes up to 15mg</td>
<td>50–200mg/day</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.15mg/kg (1mg every 2 minutes)</td>
<td>40–240mg/day</td>
</tr>
<tr>
<td>Esmolol</td>
<td>0.5mg bolus, then 0.05–0.2mg/kg per minute</td>
<td>NA</td>
</tr>
<tr>
<td>Pindolol</td>
<td>NA</td>
<td>7.5–30mg/day</td>
</tr>
<tr>
<td>Atenolol</td>
<td>5mg over 5 minutes, repeat in 10 minutes</td>
<td>25–100mg/day</td>
</tr>
<tr>
<td>Nadolol</td>
<td>NA</td>
<td>20–80mg/day</td>
</tr>
<tr>
<td><strong>Calcium channel blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td>0.075–0.15mg/kg over 2 minutes; 0.005mg/kg per minute</td>
<td>120–360mg/day</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>0.25–0.35mg/kg followed by 5–15mg/hour</td>
<td>120–360mg/day</td>
</tr>
<tr>
<td><strong>Cardiac glycoside</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.75mg–1.5mg in divided doses over 12–24 hours</td>
<td>0.125mg–0.375mg/day</td>
</tr>
</tbody>
</table>
Nonpharmacologic Therapies for rate control

- Pacemaker therapy
- Catheter ablation of AV node
- Catheter and surgical ablation

- Reserved for patients refractory to standard medical management
Pacemaker therapy

• Typically used in setting of sinus node dysfunction or AV block
• In sick sinus syndrome, atrial pacing results in much less atrial fibrillation than ventricular pacing
• In permanent atrial fibrillation, VVIR is the pacing mode of choice
• For selected patients atrial defibrillators are available to sense AF and either pace rapidly or shock to convert to sinus rhythm
Catheter ablation of AV node

• For patients resistant to medical rate control

• Requires implantation of pacemaker at time of ablation
  – VVIR mode for permanent atrial fibrillation
  – DDDR with mode switching for paroxysmal atrial fibrillation

• Must still risk stratify for thromboembolism and anticoagulate if indicated!
Surgical ablation

- Maze procedure (and variants) – multiple linear incisions in both atria, excision of both atrial appendages, and isolation of pulmonary veins
  - Complications of fluid retention, atrial arrhythmia
- Radiofrequency – lesion made on endocardium via atriotomy during open heart surgery
Pulmonary Vein Ablation (Percutaneous)

- 1,171 Symptomatic patients with symptomatic AF
- 589 to ablation, 582 to antiarrhythmic therapy (not randomized)
  - Ablation patients off coumadin after 4 weeks
  - Amiodarone, flecainide, propafenon, sotalol most common antiarrhythmics
- Median followup 900 days
- Ablation improved Mortality (92% vs 86% at 3 years), Morbidity (Heart failure, CVA, AF recurrence, and Quality of Life scores
Worldwide Survey of Atrial Fibrillation Ablation

- 181 of 777 Worldwide centers surveyed
- 1995 – 18 procedures; 2002 – 5005 procedures

Patient results
- 52% asymptomatic without drugs
- 24% asymptomatic with drugs
- 27% required >1 procedure
- 6% major complications
  - 0.05% death
  - 1.22% Tamponade
  - 0.28% Stroke
  - 1.6% Pulmonary vein stenosis

Atrial Fibrillation technique

- June 2005 German study
  - 50 patients circumferential PV ablation
  - 50 Segmental PV ablation
- Not much difference at 6 months
- Circumferential: More symptomatic Atrial Flutter
- Segmental: More pulmonary vein stenosis

Karch et. al, 2005
Rate control vs Rhythm Control

- Previous belief that maintenance of sinus rhythm improved morbidity and mortality
- Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)
  - 4060 patients, at 3.5 years trend toward lower mortality in rate control group
- 2 smaller trials also showed no stroke or mortality benefit to rhythm control
  - Pharmacological Intervention in Atrial Fibrillation (PIAF)
  - Rate Control vs. Electrical Cardioversion (RACE)
- In asymptomatic patients, either strategy is acceptable
- Lesson from trials: Anticoagulation must be continued with rhythm control
Risk of Stroke

- Thromboembolic stroke, typically due to thrombus in the left atrial appendage
- Risk of stroke 5-9% per year among high risk patients on aspirin (not coumadin)
- Duration of episodes and overall atrial fibrillation burden have not been useful to assess stroke risk
## Stroke Prevention in Atrial Fibrillation Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Time Interval</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPAF I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin vs. placebo</td>
<td>1987–1989</td>
<td>Warfarin substantially reduces stroke</td>
</tr>
<tr>
<td>Aspirin vs. placebo</td>
<td>1987–1990</td>
<td>Aspirin reduces stroke</td>
</tr>
<tr>
<td><strong>SPAF II</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin vs. aspirin, age ≤ 75 y</td>
<td>1987–1992</td>
<td>Small absolute reduction in stroke by warfarin over aspirin in unselected patients</td>
</tr>
<tr>
<td>Warfarin vs. aspirin, age &gt; 75 y</td>
<td>1989–1992</td>
<td>High rate of intracranial bleeding with warfarin (INR, 2–4.5) in patients &gt;75 years of age offset reduction in ischemic stroke</td>
</tr>
<tr>
<td><strong>SPAF III</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin INR 2–3 vs. aspirin plus low-intensity, fixed-dose warfarin in selected high-risk patients</td>
<td>1993–1995</td>
<td>Warfarin INR 2–3 offers large benefits over aspirin plus low-intensity, fixed-dose warfarin for high-risk patients</td>
</tr>
<tr>
<td>Aspirin-treated low-risk cohort</td>
<td>1993–1997</td>
<td>Patients whose stroke risk is low when given aspirin can be identified (validation of the SPAF risk stratification scheme)</td>
</tr>
</tbody>
</table>

* All were randomized trials, except the nonrandomized aspirin-treated low-risk cohort clinical trial in SPAF III, in which all participants were prescribed aspirin and followed to validate the stroke risk stratification scheme. INR = international normalized ratio; SPAF = Stroke Prevention in Atrial Fibrillation.
# SPAF 3 Risk factors

## Table 3. Stroke Prevention in Atrial Fibrillation III Stroke Risk Stratification Scheme*

<table>
<thead>
<tr>
<th>Risk Strata and Criteria</th>
<th>Ischemic Stroke with Aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Derivation Cohort (n = 854)</td>
</tr>
<tr>
<td>High risk</td>
<td>%/y</td>
</tr>
<tr>
<td>Previous stroke or transient ischemic attack</td>
<td>5.9†</td>
</tr>
<tr>
<td>Systolic blood pressure &gt; 160 mm Hg</td>
<td></td>
</tr>
<tr>
<td>Heart failure†</td>
<td></td>
</tr>
<tr>
<td>Women &gt; 75 y</td>
<td></td>
</tr>
<tr>
<td>Moderate risk</td>
<td>2.8</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>No high-risk features</td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>1.0</td>
</tr>
<tr>
<td>No hypertension</td>
<td></td>
</tr>
<tr>
<td>No high-risk features</td>
<td></td>
</tr>
</tbody>
</table>

* SPAF = Stroke Prevention in Atrial Fibrillation.
† Excluding patients with previous stroke or transient ischemic attack, the annualized rates among remaining high-risk patients with atrial fibrillation (that is, for primary prevention) were 5.8% per year for the derivation data set (27), 5.3% per year for the test cohort (6), and 3.4% per year for the other clinical trials cohort (28).
‡ Congestive heart failure within the previous 3 months or left ventricular fractional shortening of ≤ 25% by precordial echocardiography.

<table>
<thead>
<tr>
<th>Risk Strata</th>
<th>Stroke Rate with Aspirin, %/y</th>
<th>Relative Risk Reduction: Warfarin vs. Aspirin, %†</th>
<th>NNT₈‡</th>
<th>General Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous stroke or transient ischemic attack</td>
<td>10</td>
<td>60</td>
<td>17</td>
<td>Warfarin (INR, 2–3)</td>
</tr>
<tr>
<td>Primary prevention</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>&gt;4</td>
<td>55</td>
<td>35</td>
<td>Warfarin (INR, 2–3)</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>2–4</td>
<td>45</td>
<td>75</td>
<td>Warfarin or aspirin‡</td>
</tr>
<tr>
<td>Low risk</td>
<td>&lt;2</td>
<td>35</td>
<td>&gt;200</td>
<td>Aspirin (81–325 mg/d)</td>
</tr>
</tbody>
</table>

Hart
Risks of anticoagulation

- Intracranial hemorrhage – 0.1-0.3%/year
- Risk of major bleed – about 2%/year
  – 13-33% risk of death from major bleed
  – 15% risk of morbidity from major bleed
Anticoagulation Recommendations

- Anticoagulate all Valvular associated Atrial Fibrillation
- Assess risk factors (and review annually)
  - Prior TIA or stroke
  - Hypertension
  - Heart failure or Left ventricular dysfunction
  - Diabetes mellitus
  - * Clinical coronary artery disease (not included as a risk factor in ACCP guidelines)
RECOMMENDATIONS FOR ANTITHROMBOTIC THERAPY IN PATIENTS WITH AF (SEE TABLE 14)

Class I

1. Administer antithrombotic therapy (oral anticoagulation or aspirin) to all patients with AF, except those with lone AF, to prevent thromboembolism. 
   (Level of Evidence: A)

Lone AF:

2. AF Without Associated Cardiovascular Disease. In younger patients, approximately 30% to 45% of paroxysmal cases and 20% to 25% of persistent cases of AF occur as lone AF (13,15,16).
Atrial Fibrillation Prognosis

- Framingham study
  - Men: Odds ratio of death 1.5
  - Women: Odds ratio of death 1.9
- Greatest impact on those with advanced heart disease or other comorbidity
So What’s New with Atrial Fibrillation?

- Recognition of upper pulmonary veins as major Atrial fibrillation focus (foci)
- Potential for Atrial Fibrillation Ablation
  - More effective for paroxysmal or persistent atrial fibrillation, rather than chronic sustained AF (25% success)
- Better antiarrhythmics?
  - AVEO118 is a novel K+ channel blocker that prolongs atrial refractory period without affecting the ventricles
- Novel direct thrombin inhibitors
  - Ximelagatran showed efficacy equivalent to coumadin in stroke prophylaxis for atrial fibrillation (SPORTIF III, SPORTIF V trials), however the FDA advisory panel recommended against drug approval due to hepatic toxicity
- Mechanical occlusion of left atrial appendage
- “Pill in the Pocket” for paroxysmal atrial fibrillation
  - Propafenone or flecainide for outpatient, episodic use
Left Atrial Appendage

Left Ventricle
Flap Opened in Posterolateral Wall

Left Atrium and Ventricle
Sectioned with Mitral Valve Cut Away

Note: broken line indicates level of origin of tricuspid valve
Left Atrial Appendage Occlusion

WATCHMAN® LAA Filter System

Implant Face Distal to Ostium
Barbs Engage LAA Wall

Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO)

- 15 patients with AF, high risk of stroke, poor coumadin candidates
- 1 month follow-up, implant stable by TEE
Back to the patient

• A 76 year old male with hypertension and hyperlipidemia diagnosed with asymptomatic atrial fibrillation, heart rate 85
  – EKG (done)
  – Echocardiography
  – Chest Xray
  – CBC, Renal panel, TSH
  – Rate control with Beta blocker (asymptomatic)
    • Assess adequacy with exercise monitoring if needed
  – Anticoagulation with coumadin
    • May consider cardioversion after 3 weeks of anticoagulation
  – Consider ischemic workup
A few comments about Atrial Flutter
Atrial Flutter

- Digoxin, Beta Blockers, Calcium Channel blockers for rate control
- Electrical cardioversion (synchronized, 25-100J) preferred over medications
- Antiarrythmic drugs have modest effect at preventing atrial flutter
- “Typical” atrial flutter very amenable to catheter ablation
Typical Atrial Flutter

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Mechanism of Typical Atrial Flutter
References