Atrial Fibrillation: State of the Art Approach

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Disclosures

<table>
<thead>
<tr>
<th>Company</th>
<th>Type</th>
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</thead>
<tbody>
<tr>
<td>Boston Scientific</td>
<td>Speaker Honoraria</td>
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<td>St. Jude Medical</td>
<td>Speaker Honoraria</td>
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<td></td>
<td>Atrial Fibrillation Advisory Board</td>
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<td>Medtronic</td>
<td>Speaker Honoraria</td>
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<tr>
<td>Sanofi-Aventis</td>
<td>Speaker’s Bureau</td>
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<td>Corazon Consulting</td>
<td>Consultant</td>
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Objectives

- Why is atrial fibrillation such a growing concern?
- Review the current strategies for atrial fibrillation
- Review the different treatment options and the reasoning behind them
- Review emerging technology
Atrial Fibrillation
Prevalence Estimates

- AF is the most common form of arrhythmia
  - 2.3 million people in the United States
  - 4.5 million people in the European Union
- AF is associated with high rates of morbidity and mortality
  - 1 of every 6 strokes occurs in patients with AF
- It is estimated that 10-30% of patients with CHF have AF


Atrial Fibrillation: Prevalence Estimates

Tupia A. New oral anticoagulants in atrial fibrillation. EHJ 2007; 29:155-65

Atrial Fibrillation: a growing problem

Most Common Arrhythmia Admission

Cost of Atrial Fibrillation

Total annual costs for treatment of AF were estimated at US $6.65 billion
- $2.93 Billion for hospitalizations
- $1.53 billion for outpatient treatment
- $235 million for prescription drugs

Atrial Fibrillation: More danger than realized?
Atrial fibrillation is a deadly disease:
Framingham Heart Study

- 40 year follow-up patients with and without atrial fibrillation.
- Adjustment for age, hypertension, diabetes, CHF, valvular disease & myocardial infarction.
- Odds ratio for death: 1.5 in men, 1.8 in women

Circ. 1998;98:946-52

Atrial Fibrillation & Risk of Death:
Framingham Heart Study

Odds ratio for death: 1.5 in men, 1.8 in women

Circ. 1998;98:946-52

Treatment?
Needs to be Effective and Safe

- Rate Control
  - Drugs
  - Ablate and Pace
- Rhythm Control
  - Antiarrhythmic Drugs
  - Ablation
Current strategies for atrial fibrillation

ACC/AHA/ESC Practice Guidelines

ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2006 Guidelines for the Management of Patients With Atrial Fibrillation)

In August 2006, the ACC/AHA/ESC released the first revised version of the guidelines.


2006 ACC/AHA/ESC Guidelines: Updated Treatment Recommendations (Recent 2011 Guidelines are an Update)

- Changes in antithrombotic guidelines
- Current status of rate control vs rhythm control issues
- Removal of class 1A antiarrhythmic agents
- Promising role of self-administered pill-in-pocket approach
- Increasing role for catheter ablation

Current strategies for atrial fibrillation

ACC/AHA/HRS Focused Update

2011 ACC/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline)


2011 Writing Group Members:
- Janet E. Greer, MD, FACC
- Charles J. Mohler, MD, FACC
- L. Scott Levy, MD, FACC
- Stephen L. Jones, MD, FACC
- Hugh Calkins, MD, FACC
- Michael J. Melot, MD, FACC
- Edward F. Young, MD, FACC
- Michael A. Kutty, MD, FACC
- Mark A. Lewandowski, MD, FACC
- Stephen C. Kimmel, MD, FACC
- Michael H. Zareba, MD, FACC
- Wayne P. Phillips, MD, FACC
- Matthew N. Talamini, MD, FACC
- Nancy L. Karch, MD, FACC
- Jonathan C. Piccini, MD, FACC
Management of the patient with Atrial Fibrillation

Stroke/Thromboembolism Prevention

Ventricular Rate Control  Rhythm Control

New updates of note!


What are the cornerstones in the management of the patient with Atrial Fibrillation?

Stroke/Thromboembolism Prevention

Ventricular Rate Control  Rhythm Control
AFFIRM Trial – Is it Worth Struggling to Maintain NSR?
(Elderly - >65y/o, Primarily Asymptomatic, 1/3 with First Episode of AFib, Heart disease)

Rhythm Control

Rate Control

4060 pts with AFib

- No difference in mortality, stroke risk or quality of life
- More frequent hospitalization and adverse drug effects in Rhythm Control arm

“Rate Control for All?!!!”


Rhythm Control for ALL halted progress in AF treatment options…..

Clinical Application of AFFIRM applied to EVERYONE

Halted Progress!!!!!

Management of Atrial Fibrillation: Ventricular Rate Control

- AV nodal blocking medications
- Beta-adrenergic blockers
- Calcium channel blockers
- Digoxin
- Ventricular pacing
- AV nodal modification/ablation with pacemaker implantation
AV Node Ablation

**Pros**
- Improvement in symptoms, QOL, LV function
- Complete rate control
- Availability of excellent rate-responsive pacemakers
- Elimination of adverse effects and costs associated with antiarrhythmic and rate-control drugs

**Cons**
- Does not address ongoing AF
- Procedural risk (bleeding, infection, perforation)
- Small risk of sudden death post-procedure
- Pacemaker dependence: adverse effects of RV pacing
- Ongoing risk of pacemaker hardware (future extraction)
- Continued antithrombotic Rx
- Imperfect "physiologic" rate response in some patients

The Rate Control Strategy: Problems with AFFIRM

- Mean age: 69.7 +/- 9 years
  - Young patients were underrepresented
- 45% of those screened declined enrollment
  - Were highly symptomatic patients underrepresented?
- AFFIRM was not a trial of sinus rhythm versus atrial fibrillation: It was a trial of the strategy
  - 62% of "Rhythm Control" patients were in NSR
  - 35% of "Rate Control" patients were in NSR
Errors in Patient Management Due to Misinterpretation of AFFIRM Trial Results

- Dooming patient without heart disease to lifelong drug therapy and coumadin
- Not attempting cardioversion in patients with “New Onset” AF because rate control is “preferred therapy”
- Forcing patient to accept rate controlling drug side effects as “part of aging process” (fatigue, loss of mental clarity, insomnia, constipation)

AFFIRM did apply to

- Asymptomatic Patients
- Elderly Patients
- No CHF
- In THIS population:
  - Rate and rhythm control strategies result in similar outcomes with respect to
    - mortality
    - stroke
    - functional capacity
    - quality of life

Ironically . . .
Management of the patient with Atrial Fibrillation

**Stroke/Thromboembolism Prevention**

**Ventricular Rate Control**

**Rhythm Control**

Management of Atrial Fibrillation: Rhythm Control

- Antiarrhythmic drugs +/- DC cardioversion
- AF catheter ablation (PVAI)
- Atrial Segmentation
  - Surgical Maze procedure
  - Catheter Maze procedure: "Linear AF ablation"
- Pacing
  - Prevention/Suppression algorithms
  - Treatment (termination) algorithms

Antiarrhythmic Drugs for AF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug Class</th>
<th>Dosage</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flecainide</td>
<td>Class 1C</td>
<td>200-300 mg</td>
<td>Ventricular tachycardia, heart failure, proarrhythmia</td>
</tr>
<tr>
<td>Propafenone</td>
<td>Class 1C</td>
<td>450-900 mg</td>
<td>Ventricular tachycardia, heart failure, proarrhythmia</td>
</tr>
<tr>
<td>Sotalol</td>
<td>Class III</td>
<td>160-320 mg</td>
<td>Asthma, bradycardia/heart block, heart failure, torsades de pointes</td>
</tr>
<tr>
<td>Amiodarone (off-label)</td>
<td>Class III</td>
<td>100-400 mg</td>
<td>Bradycardia/heart block, thyroid dysfunction, pulmonary and liver toxicity with long-term use</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Class III</td>
<td>500-1000 mcg</td>
<td>QT interval prolongation (need to monitor), torsades de pointes, conduction disturbances</td>
</tr>
</tbody>
</table>

Dronedarone 800mg


2. Wann S et al ACC/AHA/HRS Focused update on the Management of Patients with Atrial Fibrillation. Dronedarone 800mg GI disturbance / Bradycardia / Use cautiously in Class 2-3 CHF.
**MAINTENANCE OF SINUS RHYTHM**

<table>
<thead>
<tr>
<th>No (or minimal) heart disease</th>
<th>Hypertension</th>
<th>Coronary artery disease</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dronedarone</td>
<td></td>
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<tr>
<td>Flecainide</td>
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<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Substantial LVH</th>
<th>Cardiac ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dofetilide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dronedarone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sotalol</td>
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<table>
<thead>
<tr>
<th>AMIODARONE</th>
<th>CATHETER ABLATION</th>
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</thead>
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<tr>
<td>Amiodarone</td>
<td>Catheter ablation</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Catheter ablation</td>
</tr>
</tbody>
</table>

LVH = left ventricular hypertrophy.
Fuster V et al. J Am Coll Cardiol. 2006;48:e149-246
Wann S et al Heart Rhythm vol 8 No 1 Jan 2011.

**Problem? They aren’t that effective**

*Time to recurrence of atrial fibrillation: Sotalol versus class I drugs*

<table>
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<th>Time to recurrence of atrial fibrillation: Sotalol versus class I drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>p = 0.007</em></td>
</tr>
</tbody>
</table>

Number of Recurrence (% Without Recurrence)
- Sotalol: 3 (100%), 41 (48%), 92 (39%), 97 (39%), 81 (21%), 64 (19%)
- Class I: 9 (100%), 60 (48%), 95 (37%), 92 (37%), 65 (26%), 67 (19%)

The AFFIRM First Antiarrhythmic Drug Substudy Investigators, J Am Coll Cardiol 2003;42:20-29
Copyright ©2003 American College of Cardiology Foundation. Restrictions may apply.

**Problem? They aren’t that safe**

Epstein, et al, Circ, 2004
Drugs have inherent risks for their decreased efficacy. This is your heart…

This is your heart on drugs…

ANY QUESTIONS?

You’re going to burn What? Where?

What is all this ablation about?

Dual Substrate Model of AF

Substrate for AF Initiation

Substrate for AF Maintenance

Stretch

Autonomic Tone

Inflammation

Toxins

Fibrosis

Electrical Remodelling (AF)

Modulating Factors
Pulmonary Vein Triggers Initiating Atrial Fibrillation

From Maze to PV's

Pulmonary Veins Antrum Isolation (PVAI): Circular Mapping
Pulmonary Veins Antrum Isolation (PVAI):
Circular Mapping

Before PV Antrum Isolation

After PV Antrum Isolation

Pulmonary Veins Antrum Isolation:
Circular Mapping Technique

Before PV Antrum Isolation

After PV Antrum Isolation
AF Ablation: Long term data

- N = 1,404 patients
  - 728 PAF
  - 676 non-PAF
    - 293 Persistent
    - 383 Long standing (chronic)
- 12 operators at 4 different centers
- Technique: intracardiac echo (ICE) guided circular mapping radiofrequency catheter ablation

Table 2: Freedom from All atrial and vagal/catheter ablation

<table>
<thead>
<tr>
<th>No.</th>
<th>Variables</th>
<th>Premorbid</th>
<th>NPI (%)</th>
<th>( P ) value</th>
<th>1 year</th>
<th>5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Premorbid 70%</td>
<td>66.1%</td>
<td>77.7%</td>
<td>&lt;0.001</td>
<td>71.9%</td>
<td>60.0%</td>
</tr>
<tr>
<td>2</td>
<td>Premorbid 65%</td>
<td>73.7%</td>
<td>71.8%</td>
<td>&lt;0.001</td>
<td>65.0%</td>
<td>51.3%</td>
</tr>
<tr>
<td>3</td>
<td>Total success rate</td>
<td>77.4%</td>
<td>70.9%</td>
<td>0.001</td>
<td>71.9%</td>
<td>60.0%</td>
</tr>
<tr>
<td>4</td>
<td>Catheter success rate</td>
<td>62.2%</td>
<td>62.2%</td>
<td>&lt;0.001</td>
<td>62.2%</td>
<td>62.2%</td>
</tr>
</tbody>
</table>


Figure 1

So what are the risks?
Atrial Fibrillation Ablation Complications
Perforation / Tamponade

- Intracardiac Echocardiography
- Rapid diagnosis
- Evaluate for RA / RV collapse

Pulmonary Vein Stenosis

- 1-2% Incidence
- CT Scans
  - 3 months
  - 6 months if stenosis seen at 3 months
- Angioplasty / Stenting warranted in cases >70% or if significant decrease in perfusion <25% in affected lung

Stroke

- 1-2% Incidence
- Char and/or Thrombus
- Intra-procedure echo
- Anticoagulation

Stroke
Esophageal Complications

- <25 reported in the world
- Insidious Onset
- Late presenting
  - 10-16 days (mean 12.3)
- Symptoms: Vague Gradual
  - Fever / Chills
  - Leukocytosis
  - Microcytic Anemia
  - Embolic phenomenon

AF Catheter Ablation
Complications by Age Groups

<table>
<thead>
<tr>
<th></th>
<th>Group I (&lt;50 years)</th>
<th>Group II (51-66 years)</th>
<th>Group III (&gt;60 years)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamponade/Perforation</td>
<td>none</td>
<td>1 (0.86%)</td>
<td>2 (0.2%)</td>
<td>NS</td>
</tr>
<tr>
<td>TIA</td>
<td>1 (0.09%)</td>
<td>none</td>
<td>1 (0.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke</td>
<td>none</td>
<td>none</td>
<td>3 (0.3%)</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Severe PV Stenosis</td>
<td>2 (1.8%)</td>
<td>3 (2.6%)</td>
<td>1 (0.9%)</td>
<td>NS</td>
</tr>
</tbody>
</table>


AF Catheter Ablation: Cleveland Clinic
Multivariate Predictors of AF Recurrence Post PVAI

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio &amp; 95% CI</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>Scar</td>
<td>0.01</td>
<td></td>
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<tr>
<td>Age (per decade)</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>EF (per 10%)</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>LA size (per cm)</td>
<td>0.95</td>
<td></td>
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<tr>
<td>Structural HD</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>AF duration</td>
<td>0.95</td>
<td></td>
</tr>
</tbody>
</table>

When do you go to ablation?

- Though these risks are low, the invasiveness of the procedure still keeps it as second line therapy
- ACC guidelines place ablation as second line therapy following an attempt at antiarrhythmic therapy

AF Catheter Ablation: Candidates

- Symptomatic AF (paroxysmal or persistent)
- At least one antiarrhythmic medication failure
- Younger patients with “lone” paroxysmal AF are the best candidates, but patients with persistent AF, older patients and those with co-morbidities such as structural heart disease and heart failure may also be appropriate candidates

AF Catheter Ablation: Potentially Poor Candidates

- Asymptomatic or minimally symptomatic AF
- No trial of antiarrhythmic drug
- Left atrial cardiomyopathy
- Goal of undergoing ablation is to get off warfarin
- Frail, elderly patients
- Severe structural heart disease, mechanical mitral valve, etc.
Emerging technologies
The quest for safer/easier/faster/better.....

- Think about it.....
  - Making it easier for the operator
    - Remote Navigation
  - Making it easier to get the lesions placed
    - Catheter shapes and sizes
    - Imaging technology
  - Making lesions safer
    - Energy Sources

Conclusions
- Atrial fibrillation is a growing problem both medically and economically
- Guidelines focus on three cornerstones of therapy
  - Thromboembolic / Stroke prevention
  - Ventricular Rate Control
  - Rhythm Control

Conclusions
- Rhythm Control
  - Medications remain first line therapy
  - Ablation therapy has demonstrated decent results at the cost of some risk
    - Individual patient evaluation and selection is critical for best results
    - Emerging therapies focus on making the procedure easier (less operator dependent) and safer.