Relevant Advances in Atrial Fibrillation

- Stroke Prophylaxis
- Antiarrhythmic Drug Therapy
- Ablation
Epidemiology

- AF is the most common sustained arrhythmia in adults
- It affects at least 2.3 million Americans
  - Expected to affect > 4 million by 2030
- Affects ~4% of everyone over age 60 and ~10% of everyone over age 80
- The age-adjusted incidence is increasing\(^1\)

1. Miyasaka Y. Circulation 2006;114:119-125

Atrial Fibrillation and Stroke

- AF is the most common cause of embolic stroke\(^1\)
- 15% of all strokes in the US can be attributed to AF\(^1\)
- AF is associated with an increase in mortality, from 1.3-2 times\(^2\)

Anticoagulation in AF
Who needs it?

• **Warfarin has been the most effective available therapy to prevent stroke in patients with AF**
  - 5 RCT of vit K antagonists v. placebo highly significant risk reduction in stroke of 62% (95% CI 48% to 72%)\(^1\)
  - Strokes on warfarin are significantly less severe\(^2\)
  - Warfarin reduced overall mortality in AF patients\(^2\)

2. Chest 2004;126:429S-456S)
3. Eur Heart J 2005;7:C12-18

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Anticoagulation in AF
Who needs it?

• **Warfarin is not perfect**
  - Significantly increase major bleeding (0.9% to 2.2%) and intracerebral hemorrhage (0.2% to 0.4%)\(^1\)

1. Eur Heart J 2005;7:C12-18
Problems with Warfarin

• Unpredictable pharmacokinetics
  – Requires monitoring, frequent blood draws
  – Requires frequent dose adjustments
• Drug-drug interactions
  – Digoxin and amiodarone commonly problematic
• Several days onset and offset
  – Often requires “bridging” with heparin
• Food interactions
  – Vitamin K (green leafy vegetables)

Direct Thrombin Inhibitor: Dabigatran (Pradaxa)

• Predictable pharmacokinetics
  – Does not require monitoring, frequent blood draws
  – Does not require dose adjustments
• Drug-drug interactions (minimal versus warfarin)
  – DECREASE: rifampin, carbamazepine
  – INCREASE: verapamil
• Does not take several days onset and offset
  – Directly inhibits thrombin, so may not require bridging
• Food interactions
  – Not related to vitamin K, so no known important food interactions
Dabigatran

• Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) study\textsuperscript{1}
  – A randomized trial that compared the blinded administration of two fixed doses of dabigatran to open-labeled use of warfarin in patients with AF and at least one additional risk factor for stroke

• 18,113 AF patients were followed for a median of 2.0 years


\begin{tabular}{|l|l|l|}
\hline
 & Dabigatran 110 mg 2x day & Dabigatran 150 mg 2xday* \\
\hline
Efficacy & Non-inferior (p<0.001) & Superior (RR 0.86, p<0.001) \\
\hline
Hemorrhagic stroke & Less (RR 0.31, p<0.001) & Less (RR 0.26, p<0.001) \\
\hline
All major bleeding & Less (RR 0.80, p=0.003) & Similar \\
\hline
GI bleeding & Not specified-apparently less & More \\
\hline
\end{tabular}

\*FDA approved

Dabigatran v Warfarin in RE-LY

- Significantly more dabigatran patients complained of dyspepsia (11-12% versus ~6%)
  - A low pH is required to enhance absorption of dabigatran
  - The dabigatran capsules contain dabigatran-coated pellets with a tartaric acid core
  - What will happen in those on H2-blockers or PPIs?

- 80% of the active drug is excreted by the kidneys
  - Using pharmacokinetic modeling, the FDA approved a 75 mg dose for those with low GFR (< 30 mL/min >15 mL/min)


American Heart Association
Learn and Live...


<table>
<thead>
<tr>
<th>2011 Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td></td>
</tr>
<tr>
<td>1. Dabigatran is useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure (creatinine clearance &lt;15 mL/min), or advanced liver disease (impaired baseline clotting function).</td>
<td>New recommendation</td>
</tr>
</tbody>
</table>

Circulation published online Feb 14, 2011
Dabigatran v Warfarin
Other Issues

• No current reversal agent for dabigatran
  – Can be removed with hemodialysis

• Cost
  – Company will supplement for the first year

Factor Xa Inhibitors

Manesh R. Patel, M.D., Kenneth W. Mahaffey, M.D., Jyotsna Garg, M.S.,
Guohua Pan, Ph.D., Daniel E. Singer, M.D., Werner Hacke, M.D., Ph.D.,
Günter Breithardt, M.D., Jonathan L. Halperin, M.D., Graeme J. Hankey, M.D.,
Jonathan P. Piccini, M.D., Richard C. Becker, M.D., Christopher C. Nessel, M.D.,
John F. Paoletti, M.D., Ph.D., Scott D. Berkowitz, M.D.,
Keith A.A. Fox, M.B., Ch.B., Robert M. Califf, M.D.,
and the ROCKET AF Steering Committee, for the ROCKET AF Investigators

Apixaban versus Warfarin in Patients with Atrial Fibrillation  N Engl J Med 2011
Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S.,
John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H.,
Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Arsheim, M.D., Dan Atar, M.D.,
Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D.,
J. Donald Easton, M.D., Justin A. Ezekowitz, M.B., B.Ch., Greg Flaker, M.D.,
David Garcia, M.D., Margarida Geraldes, Ph.D., Bernard J. Gersh, M.D.,
Sergey Golitsyn, M.D., Ph.D., Shinya Goto, M.D., Antonino G. Hermosillo, M.D.,
Stefan H. Hohloser, M.D., John Horowitz, M.D., Puneet Mohan, M.D., Ph.D.,
Pet Jansky, M.D., Basil S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Przemyslaw M.D.,
Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D.,
and Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators
### Factor Xa Inhibitors

<table>
<thead>
<tr>
<th></th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial name</strong></td>
<td>ROCKET AF</td>
<td>ARISTOTLE</td>
</tr>
<tr>
<td><strong>Support</strong></td>
<td>J&amp;J and Bayer</td>
<td>Bristol-Myers Squibb and Pfizer</td>
</tr>
<tr>
<td><strong>Data analysis/ manuscript</strong></td>
<td>Duke</td>
<td>Duke and Bristol-Myers Squibb</td>
</tr>
<tr>
<td><strong>Number enrolled</strong></td>
<td>14,264</td>
<td>18,201</td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td>AF CHADS$_2 \geq 2$</td>
<td>AF CHADS$_2 \geq 1$</td>
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</table>

### Dosing

<table>
<thead>
<tr>
<th></th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
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<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>20 mg once daily v. warfarin (blinded)</td>
<td>5 mg twice daily v. warfarin (blinded)</td>
</tr>
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</table>

### Renal adjustments

<table>
<thead>
<tr>
<th></th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Renal adjustments</strong></td>
<td>15 mg daily if GFR 30-49 ml/min</td>
<td>2.5 mg twice daily if two or more: age &gt; 80, weight &lt; 60 kg or Cr &gt; 1.5 (25% renal excretion).</td>
</tr>
</tbody>
</table>

Excluded if Cr > 2.5
<table>
<thead>
<tr>
<th></th>
<th>Rivaroxaban ROCKET AF</th>
<th>Apixaban ARISTOTLE</th>
<th>Dabigatran RE-LY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of time with</td>
<td>55%</td>
<td>62%</td>
<td>64%</td>
</tr>
<tr>
<td>therapeutic INR in the</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>warfarin group</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Per protocol:**
- 1.7% per year v. 2.2% per year (p<0.001 for noninferiority)

**Intention to treat:**
- p<0.001 for noninferiority, p=0.12 for superiority
• Major GI bleeding was more common with rivaroxaban (3.2% versus 2.2%, p<0.001).
• No mention of more dyspepsia
• More epistaxis and hematuria with rivaroxaban mentioned in appendix
• In intention to treat, death occurred in 4.5% of rivaroxaban group v. 4.9% of warfarin group (p=0.15)
• No meaningful differences across various subgroups or time with therapeutic INR
Efficacy (Intention to treat):
1.27% per year v. 1.60% per year
(p<0.01 for superiority)

SAFETY (Intention to treat):
2.13% per year v. 3.09% per year p<0.001 for superiority

Table 3. Bleeding Outcomes and Net Clinical Outcomes. *

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Apixaban Group (N=3883)</th>
<th>Warfarin Group (N=4052)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage</td>
<td>Patients with Event</td>
<td>Event Rate</td>
<td>Patients with Event</td>
<td>Event Rate</td>
</tr>
<tr>
<td>Intracranial</td>
<td>127</td>
<td>2.13</td>
<td>122</td>
<td>0.80</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>605</td>
<td>0.76</td>
<td>977</td>
<td>0.92</td>
</tr>
<tr>
<td>Major or clinically relevant non-maj. bleeding</td>
<td>4052</td>
<td>0.52</td>
<td>172</td>
<td>1.33</td>
</tr>
<tr>
<td>TIMI major bleeding</td>
<td>148</td>
<td>0.66</td>
<td>256</td>
<td>1.69</td>
</tr>
<tr>
<td>TIMI minor bleeding</td>
<td>249</td>
<td>1.55</td>
<td>370</td>
<td>2.46</td>
</tr>
<tr>
<td>Any bleeding</td>
<td>2156</td>
<td>18.1</td>
<td>3960</td>
<td>25.3</td>
</tr>
</tbody>
</table>

* The bleeding outcomes were assessed in patients who received at least one dose of a study drug and events that occurred from the time the patients received the first dose of the study drug through 2 days after they received the last dose. The net clinical outcome includes all efficacy outcomes through the cutoff date for the efficacy analysis and bleeding outcomes that occurred from the time the patients received the first dose of the study drug through 2 days after they received the last dose. GUSTO denotes Global Use of Strategies to Open Occluded Coronary Arteries, and TIMI Thrombolysis in Myocardial Infarction.

**The comparison of the primary safety outcome of bleeding according to the International Society on Thrombosis and Haemostasis (ISTH) criteria is to the hierarchical sequence preserving a type I error.
**Apixaban ARISTOTLE**

- Rate of death with Apixaban was 3.52% per year versus 3.94% per year with warfarin (p=0.047).
  - Similar magnitude reduction in RE-LY, p=0.051
  - Similar magnitude reduction in point estimate in ROCKET AF, but p=0.15
- No meaningful differences across various subgroups
- Dyspepsia apparently not an issue

**Factor Xa Inhibitors**

- Efficacy appears to be as good or better than warfarin.
- Bleeding risk appears to be similar or less
- Lower risk of hemorrhagic stroke
  - Suggestion that inhibition of factor VII by warfarin may result in particularly potent anticoagulation in the CNS
- No evidence of LFT abnormalities
- No evidence of dyspepsia
Factor Xa Inhibitors

- Renal disease patients need to be considered carefully
- ENGAGE AF-TIMI 48 results are pending
- No reversal agents
- Cardioversion/ablation patients
  - Can we count on a history of regular dosing?
  - Should we still do a TEE?

Anticoagulation in AF
Who needs it?

- Aspirin has some efficacy versus placebo, but inferior to warfarin\(^1\)
  - Less bleeding risk

Anticoagulation in AF
Who needs it?

CHADS 2 score:
1 point for:
   CHF (or reduced systolic function), HTN,
   age ≥ 75 years, DM
2 points for:
   History of stroke or TIA
0-1: low risk
2-3: moderate risk
4-6: high risk

1. JAMA 2001;285:2864-2870

Anticoagulation- who needs it?

• Class I: If more than one risk factor→ warfarin or dabigatran

• Class IIa: If just one risk factor, depending on assessment of bleeding risk, ability to safely administer, and patient preference → aspirin (81-325 mg) or warfarin or dabigatran

• Class IIa: If one or more “less well established” risk factors: age 66-74, female gender, or CAD → aspirin or warfarin or dabigatran

Factor et al.
ACC/AHA/ESC Practice Guidelines
JACC Vol. 49, No. 4, 2007
Aug 21, 2007: e149-e246
Anticoagulation - extra tid-bit

- Class III: Long-term vitamin K antagonists (and presumably dabigatran) are not recommended for primary prevention of stroke in patients younger than 60 without heart disease...
I decide to go with

- Most thrombi in atrial fibrillation arise from the left atrial appendage
- Cardioversion can reduce left atrial appendage function
  -- Even from AF to sinus
- The pericardioversion period is a particularly pro-thrombotic time
  -- Regardless of mode: DC/ electrical, pharmacologic, spontaneous

I decide to go with

- Prior to cardioversion:¹ ²
  -- Can exclude preexisting thrombus by TEE
  -- Can anticoagulate (therapeutic/for at least 3 weeks) prior to cardioversion

1. JACC 2006;48:e149-246
2. Chest 2004;126:429S-456
I decide to go with

- During and after cardioversion: ¹, ²
  -- Anticoagulation for at least 4 weeks
  -- Applies even to those who would otherwise not require anticoagulation
- The magic 48 hours
  -- Must be documented!
  1. JACC 2006;48:e149-246
  2. Chest 2004;126:429S-456

Devices for stroke prevention

- All anticoagulants by nature will be associated with an increased risk of bleeding
- In AF patients with thrombus/thromboembolism, the left atrial appendage is thought to be the site of thrombus formation in more than 90%
The Watchman Device

A self-expanding nickel titanium (nitinol) frame structure with fixation barbs and a permeable polyester fabric cover implanted via a trans-septal approach to seal the left atrial appendage\(^1\)

Fountain RB et al. Am Heart J 2006

The Watchman Device

• PROTECT AF randomized 707 AF patients with an additional risk factor in a 2:1 ratio to percutaneous closure of the left atrial appendage or warfarin therapy
• The device was successfully implanted in 88% of those assigned to the intervention.
  – At the pre-specified 45-day follow-up, 86% of the device patients had a transesophageal echocardiogram (TEE) that met the predefined criteria necessary to discontinue warfarin.
  – After stopping warfarin, participants with the device were prescribed clopidogrel 75 mg daily and aspirin 81 mg daily. The clopidogrel was stopped after the 6-month follow-up visit.

Holmes DR et al. Lancet 2009
The Watchman Device

- After 18 ± 10 months of follow-up, the primary efficacy rate of stroke, cardiovascular or unexplained death, or systemic embolism was non-inferior to warfarin.
- Ischemic strokes were more common in the intervention group, and hemorrhagic strokes were more common in the warfarin group.
- Complications of the device implant procedure:
  - serious pericardial effusion in 22 (4.8%),
  - procedure-related ischemic stroke attributed to air embolism in 5 (1.1%)
  - Device embolization in 3 (0.6%).

Holmes DR et al. Lancet 2009

The Watchman Device

- When the analysis was restricted to only those in the intervention group that had successful device implantation allowing for warfarin discontinuation, the device was found to be superior for the primary efficacy endpoint.
- Good proof of principal, but:
  - Could not be successfully implanted in everyone
  - Still needed warfarin for > 1 month

Holmes DR et al. Lancet 2009
PLACE™
Percutaneous Left Auricle Closure & Exclusion
Feasibility of closed-chest ligation of the left atrial appendage in humans

Krzysztof Bartus, MD, PhD,* Jacek Bednarek, MD, PhD;† Jacek Myc, MD,* Boguslaw Kapelak, MD,* Jerzy Sadowski, MD, PhD,* Jacek Lebowski, MD,*† Steven J. Yakubov, MD,†

Randall J. Lee, MD, PhD†,§

From the *Department of Cardiovascular Surgery and Transplantology and the †Department of Electrophysiology, Jagiellonian University, John Paul II Hospital in Krakow, Poland; ‡Riverside Methodist Hospital, Columbus, Ohio; and §Cardiovascular Research Institute, Department of Medicine, and †Institute for Regenerative Medicine, University of California San Francisco, San Francisco, California.

- 13 patients
  - 2 undergoing mitral valve surgery confirmed closure by visual inspection
  - 1 unsuccessful during case
  - 1 requiring surgery because concave septum compressed the LARIAT

Catheter-Based Left Atrial Appendage (LAA) Ligation for the Prevention of Embolic Events Arising From the LAA Initial Experience in a Canine Model

Randall J. Lee, MD, PhD; Krzysztof Bartus, MD; Steven J. Yakubov, MD

Catheter-Based Left Atrial Appendage (LAA) Ligation for the Prevention of Embolic Events Arising From the LAA: Initial Experience in a Canine Model

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Feasibility of closed-chest ligation of the left atrial appendage in humans

Krzysztof Bartun, MD, PhD,* Jacek Bednarek, MD, PhD,† Jacek Wyc, MD,* Boguslaw Kapelak, MD,* Jerzy Sadowski, MD, PhD,* Jacek Lejnakowski, MD,† Steven J. Yakubov, MD,† Randall J. Lee, MD, PhD*†

From the *Department of Cardiovascular Surgery and Transplantology and the †Department of Electrophysiology, Jagiellonian University, John Paul II Hospital in Krakow, Poland; ‡Riverside Methodist Hospital, Columbus, Ohio, and §Institute for Regenerative Medicine, University of California San Francisco, San Francisco, California.

11/2/11

• 13 patients
• 2 undergoing mitral valve surgery confirmed closure by visual inspection
• 1 unsuccessful during case
• 1 requiring surgery because concave septum compressed the LARIAT

PATIENTS SCREENED
N=119

PATIENTS EXCLUDED
N=16 (13.4%)

LAA Width ≥40mm
N=8 (6.7%)

Unsuitable LAA Orientation
N=8 (6.7%)

ELIGIBLE PATIENTS
N=103 (86.5%)

Presence of Adhesions
N=3 (2.9%)

Mobile Thrombus*
N=11 (10.6%)

EXCLUDED AT TIME OF PROCEDURE
N=14 (13%)

PATIENTS TO BE TREATED
N=89 (80.4%)

FAILURE TO TREAT
N=4 (4.5%)

SUCCESSFUL LAA CLOSURE
N=85 (95.5%)

PT 9: Pericardial effusion due to inadvertent RV dilation
PT 24: Pericardial effusion at initiation due to epigastric nick
PT 25: Anatomic contraindication prior to transseptal (dilated RA)
PT 93: Unable to capture LAA due to localized adhesions on LAA sulcus

* Mobile thrombus considered a temporary exclusion. Patients placed on OAC until resolved and treated 30-60 days later.
Appendage Closure Devices and the Guidelines

- No guidelines for now

- Likely indicated for:
  - If CHADS2 score warrants warfarin or dabigatran (Pradaxa) and there are contraindications (mainly bleeding)
  - If patient has a stroke on warfarin or dabigatran (Pradaxa)
Conclusions: Stroke and AF

• Competition will likely be a good thing for patients and doctors

• Payers will need to recognize the benefits of these new drugs so we can deliver them to our patients

• Devices for left atrial appendage exclusion appear to be feasible and may be considered for AF patients at high risk for stroke that are unsuitable for anticoagulation alone
Amiodarone has best efficacy

Dronedarone:

1. Elevation of serum creatinine more common versus placebo
2. May increase mortality in severe heart failure patients (ANDROMEDA).¹
3. Reduced cardiovascular hospitalization or death in AF patients with at least one other cardiovascular risk factor (ATHENA).²
4. Evidence that dronaderone is less efficacious than amiodarone (DIONYSOS).³

¹ Kober et al. NEJM 2008
² Hohnloser et al. NEJM 2008
³ Le Heuzey JY et al. JCE 2010
PALLAS
Permanent Atrial fibrillation outcome Study using dronedarone on top of standard therapy

- Randomized, Double Blind, Placebo Controlled, Trial for Assessing the Clinical Benefit of Dronedarone 400mg BID in Patients With Permanent Atrial Fibrillation and Additional Risk Factors
PALLAS

• Inclusion criteria:
  – Permanent AF
  – At least one:
    • Coronary artery disease
    • Prior stroke or Transient Ischemic Attack (TIA)
    • Symptomatic heart failure
    • Left ventricular ejection fraction \( \leq 0.40 \)
    • Peripheral arterial occlusive disease
    • Aged 75 years or older with both hypertension and diabetes mellitus

PALLAS

• Exclusion criteria:
  – Paroxysmal AF
  – Persistent AF without a decision to allow AF to continue without further efforts to restore sinus rhythm
  – Heart failure of New-York Heart Association (NYHA) class IV or recent unstable NYHA class III
PALLAS: Halted Early

<table>
<thead>
<tr>
<th>Event</th>
<th>Multaq N=1572</th>
<th>Placebo N=1577</th>
<th>Hazard Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV Death, Myocardial Infarction, Stroke,</td>
<td>32 (2)</td>
<td>14 (0.9)</td>
<td>2.3</td>
<td>0.009</td>
</tr>
<tr>
<td>Systemic Embolism*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>118 (7.5)</td>
<td>81 (5.1)</td>
<td>1.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Unplanned CV Hospitalization*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>16 (1)</td>
<td>7 (0.4)</td>
<td>2.3</td>
<td>0.065</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>3 (0.2)</td>
<td>3 (0.2)</td>
<td>1.0</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>17 (1.1)</td>
<td>7 (0.4)</td>
<td>2.4</td>
<td>0.047</td>
</tr>
<tr>
<td>Heart Failure Hospitalization</td>
<td>34 (2.2)</td>
<td>15 (1)</td>
<td>2.3</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* Primary endpoint

From the FDA

- Do not prescribe Multaq to patients with permanent atrial fibrillation
- FDA is evaluating whether and how the preliminary results of the PALLAS study apply to patients taking Multaq for paroxysmal or persistent atrial fibrillation (AF) or atrial flutter (AFL)
- The PALLAS study results are considered preliminary at this time because the data have not undergone quality assurance procedures and have not been completely adjudicated
- Report adverse events involving dronedarone to the FDA MedWatch program
Atrial Fibrillation Ablation

- High success (> 90-95%) and low risk (< 1%):
  - AV nodal ablation and pacemaker
  - Atrial flutter ablation
  - SVT ablation
Atrial Fibrillation Ablation

- Lower success (60-90%) and higher risk (4-6%):¹⁻⁵
  - Atrial fibrillation ablation

2. JACC 2003;42:185-197
3. JACC 2004;43:2044-53
4. JAMA 2005;293:2634-40
Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation: A Randomized Controlled Trial

Figure 2. Kaplan-Meier Curves of Time to Protocol-Defined Treatment Failure, Recurrence of Symptomatic Atrial Arrhythmia, and Recurrence of Any Atrial Arrhythmia by Treatment Group

<table>
<thead>
<tr>
<th>Feature</th>
<th>Catheter Ablation</th>
<th>Antiarrhythmic Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>100</td>
<td>50</td>
</tr>
<tr>
<td>Heart rate (pre-ablation)</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td>Heart rate (post-ablation)</td>
<td>57</td>
<td>57</td>
</tr>
</tbody>
</table>

Class I

2. Catheter ablation performed in experienced centers is useful in maintaining sinus rhythm in selected patients with significantly symptomatic, paroxysmal AF who have failed treatment with an antiarrhythmic drug and have normal or mildly dilated left atria, normal or mildly reduced LV function, and no severe pulmonary disease.30-31 (Level of Evidence: A)

Modified recommendation (class of recommendation changed from IIa to I, wording revised, and level of evidence changed from C to A).
Class Ila

6. Catheter ablation is reasonable to treat symptomatic persistent AF \(^{28,48,50-64}\) \((\text{Level of Evidence: A})\)

New recommendation

Class IIb

1. Catheter ablation may be reasonable to treat symptomatic paroxysmal AF in patients with significant left atrial dilation or with significant LV dysfunction \(^{28,48,50-64}\) \((\text{Level of Evidence: A})\)

New recommendation
Atrial Fibrillation Ablation

- Best candidates:
  - Paroxysmal AF
  - Symptomatic
  - Failed at least one antiarrhythmic drug
  - The younger and healthier, the better

Atrial Fibrillation Ablation

- Ablation Versus Anti-Arrhythmic (AA) Drug Therapy for AF - Pivotal Trial (CABANA)

- NHLBI, St. Jude and Biosense Webster sponsored study designed to compare mortality in AF ablation versus medical treatment

ClinicalTrials.gov
Conclusions

• Stroke prophylaxis must always be considered
  – The options tailored to the individual patient

• Dronaderone (Multaq) is a new option for antiarrhythmic therapy
  – Not clearly superior to other alternatives
  – Recent concerns regarding safety

• Ablation should be considered in the symptomatic patient who has failed antiarrhythmic therapy.

Thank You