Atrial fibrillation
How is treatment changing?

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Director, Electrophysiology Service
1 February 2014
Outline

• Introduction
• Natural history of afib and stroke
• Current risk stratification
  – CHADS
  – CHADS-VASc
  – HAS-BLED
• New oral anticoagulants
  – Dabigatran
  – Rivaroxaban
  – Apixaban
• Afib management and ablation
• Left atrial appendage closure
Atrial Fibrillation

- Lack of organized electrical activity in the atria
- Electrical “noise”
- Irregular conduction of impulses through the AV node
- Irregularly irregular HR
Atrial fibrillation types

• Paroxysmal
  – Atrial fibrillation that stops spontaneously
    • Episodes may occur rarely or several times per day
    • Episodes may last seconds to days

• Persistent
  – Atrial fibrillation that is always present

• Longstanding persistent
  – Continuously present for at least 6 months

• Permanent
  – Continuously present for at least 6 months and no efforts are made to restore sinus rhythm
AF Is the Leading Cause of Hospitalizations for Arrhythmia

Hospital Admissions in US

- AF
- AFL
- Cardiac arrest
- Conduction disease
- Junctional
- Premature beats
- Sick sinus
- Unspecified
- VF
- VT

N=517,699 (representing 10% of CV admissions).

VF, ventricular fibrillation; VT, ventricular tachycardia.

AF Is Associated With Increased Thromboembolic Risk

- Major cause of stroke in elderly\(^1\)
- 5-fold ↑ in risk of stroke\(^1,2\)
- 15% of strokes in US are attributable to AF\(^3\)
- Stroke severity (and mortality) is worse with AF than without AF\(^4\)
- Incidence of all-cause stroke in patients with AF: 5%\(^1\)
- Stroke risk persists even in asymptomatic AF\(^5\)

Atrial Fibrillation
Why do we treat it?

• Risk of stroke
  – No organized mechanical function of the atria
  – Blood pooling and low flow → clots

• Symptoms
  – Huge range: asymptomatic to very disabled
  – Palpitations, shortness of breath, decreased energy

• Generally not a sign of other cardiac disease
  – Exception is chronically elevated heart rate, leading to tachycardia-induced cardiomyopathy
Cumulative Mortality from Any Cause in the Rhythm-Control Group and the Rate-Control Group

![Graph showing cumulative mortality over time for rhythm control and rate control groups. The graph includes a table with the number of deaths in each group over different years, with a significance level of P=0.08.]

Atrial fibrillation
Anticoagulation

• Old paradigm:
  – Lone afib
    • Under age 65
    • Paroxysmal
    • No other medical problems
    • Aspirin is sufficient
  – Everyone else needed warfarin

• New Paradigm:
  – Use risk scores to determine need for warfarin
CHADS2 score

- Congestive heart failure
- Hypertension
- Age > 75 years
- Diabetes Mellitus
- Stroke

- If CHADS2 = 0  low risk of CVA (ASA)
- If CHADS2 = 1, moderate risk of CVA (ASA or warfarin)
- If CHADS2 >=2, higher risk of CVA (warfarin)
Table 2. Risk of Stroke in National Registry of Atrial Fibrillation (NRAF) Participants, Stratified by CHADS$_2$ Score*

<table>
<thead>
<tr>
<th>CHADS$_2$ Score</th>
<th>No. of Patients (n = 1733)</th>
<th>No. of Strokes (n = 94)</th>
<th>NRAF Crude Stroke Rate per 100 Patient-Years</th>
<th>NRAF Adjusted Stroke Rate, (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>120</td>
<td>2</td>
<td>1.2</td>
<td>1.9 (1.2-3.0)</td>
</tr>
<tr>
<td>1</td>
<td>463</td>
<td>17</td>
<td>2.8</td>
<td>2.8 (2.0-3.8)</td>
</tr>
<tr>
<td>2</td>
<td>523</td>
<td>23</td>
<td>3.6</td>
<td>4.0 (3.1-5.1)</td>
</tr>
<tr>
<td>3</td>
<td>337</td>
<td>25</td>
<td>6.4</td>
<td>5.9 (4.6-7.3)</td>
</tr>
<tr>
<td>4</td>
<td>220</td>
<td>19</td>
<td>8.0</td>
<td>8.5 (6.3-11.1)</td>
</tr>
<tr>
<td>5</td>
<td>65</td>
<td>6</td>
<td>7.7</td>
<td>12.5 (8.2-17.5)</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>2</td>
<td>44.0</td>
<td>18.2 (10.5-27.4)</td>
</tr>
</tbody>
</table>

*CHADS$_2$ score is calculated by adding 1 point for each of the following conditions: recent congestive heart failure, hypertension, age at least 75 years, or diabetes mellitus and adding 2 points for having had a prior stroke or transient ischemic attack. CI indicates confidence interval.

†The adjusted stroke rate is the expected stroke rate per 100 patient-years from the exponential survival model, assuming that aspirin was not taken.

Double the CHADS2 score = the annual risk of stroke
CHADS\textsubscript{a}V\textsubscript{a}S\textsubscript{c} score

- Congestive heart failure 1
- Hypertension 1
- Age > 75 2
- Diabetes 1
- Stroke/TIA 2
- Vascular disease 1
- Age 65-75 1
- Sex category (female) 1
CHADSVASc score

- Score  •  Annual stroke risk
- 0      • 0
- 1      • 1.3%
- 2      • 2.2%
- 3      • 3.2%
- 4      • 4.0%
- 5      • 6.7%
- 6      • 9.8%
- 7      • 9.6%
- 8      • 6.7%
- 9      • 15.2%
HASBLED score

- Hypertension
- Abnormal renal and liver function
- Stroke
- Bleeding (major prior)
- Labile INRs
- Elderly (>65 years)
- Drugs or alcohol

- Used to assess bleeding risk, if >3 anticoagulate with caution
Choices in anticoagulation

• Warfarin
  – Narrow therapeutic window
    • Requires regular check of the INR
  – Vast experience
  – “rat poison”
  – We all have long been waiting for an alternative

• New choices
  – Dabigatran (direct thrombin inhibitor)
  – Rivaroxaban (factor XA inhibitor)
  – Apixaban (factor XA inhibitor)
Contact Phase

Site of Action of Heparin

Site of Action of Warfarin

Site of action of dabigatran

Site of action of rivaroxaban and apixaban
Dabigatran
(Pradaxa)

• Direct thrombin inhibitor
• Approved in 2010 for treatment of non-valvular afib at 150mg BID dose
• No monitoring of effect
• Significant GI distress in some patients
RE-LY trial
dabigatran

• 18,113 patients
  – Atrial fibrillation
  – Another risk factor for stroke
• Randomized to
  – warfarin v.
  – dabigatran (110 or 150mg BID)
• Primary outcome stroke or systemic embolism
Cumulative Hazard Rates for the Primary Outcome of Stroke or Systemic Embolism, According to Treatment Group.

RE-LY (dabigatran)

## Table 3. Safety Outcomes, According to Treatment Group.

<table>
<thead>
<tr>
<th>Event</th>
<th>Dabigatran, 110 mg</th>
<th>Dabigatran, 150 mg</th>
<th>Warfarin</th>
<th>Dabigatran, 110 mg, vs. Warfarin</th>
<th>Dabigatran, 150 mg, vs. Warfarin</th>
<th>Dabigatran, 150 mg vs. 110 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients</td>
<td>%/yr</td>
<td>no. of patients</td>
<td>%/yr</td>
<td>no. of patients</td>
<td>%/yr</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>322</td>
<td>2.71</td>
<td>375</td>
<td>3.11</td>
<td>397</td>
<td>3.36</td>
</tr>
<tr>
<td>Life threatening</td>
<td>145</td>
<td>1.22</td>
<td>175</td>
<td>1.45</td>
<td>212</td>
<td>1.80</td>
</tr>
<tr>
<td>Non–life threatening</td>
<td>198</td>
<td>1.66</td>
<td>226</td>
<td>1.88</td>
<td>208</td>
<td>1.76</td>
</tr>
<tr>
<td>Gastrointestinal†</td>
<td>133</td>
<td>1.12</td>
<td>182</td>
<td>1.51</td>
<td>120</td>
<td>1.02</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>1566</td>
<td>13.16</td>
<td>1787</td>
<td>14.84</td>
<td>1931</td>
<td>16.37</td>
</tr>
<tr>
<td>Major or minor bleeding</td>
<td>1740</td>
<td>14.62</td>
<td>1977</td>
<td>16.42</td>
<td>2142</td>
<td>18.15</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td>27</td>
<td>0.23</td>
<td>36</td>
<td>0.30</td>
<td>87</td>
<td>0.74</td>
</tr>
<tr>
<td>Extracranial bleeding</td>
<td>299</td>
<td>2.51</td>
<td>342</td>
<td>2.84</td>
<td>315</td>
<td>2.67</td>
</tr>
<tr>
<td>Net clinical benefit outcome</td>
<td>844</td>
<td>7.09</td>
<td>832</td>
<td>6.91</td>
<td>901</td>
<td>7.64</td>
</tr>
</tbody>
</table>

* Data are shown for all patients who had at least one event. All analyses were based on the time to the first event. Hemorrhagic stroke was a subcategory of stroke in the efficacy analysis and in the safety analysis is also counted as major, life-threatening bleeding and as part of intracranial bleeding.
† Gastrointestinal bleeding could be life threatening or non–life threatening.
‡ The net clinical benefit outcome was the composite of stroke, systemic embolism, pulmonary embolism, myocardial infarction, death, or major bleeding.

Rivaroxaban
(Xarelto)

- Direct factor XA inhibitor
- Approved in 11/2011 for non-valvular atrial fibrillation
- QD dosing
- Rare side effects
- Rebound hypercoagulant effect?
Rocket-AF trial
rivaroxaban

- 14,264 patients
  - Atrial fibrillation
  - CHADS2 score of \( \geq 2 \)
- Randomized to
  - Warfarin v.
  - Rivaroxaban 20mg QD
- Primary outcome stroke or systemic embolism
Cumulative Rates of the Primary End Point (Stroke or Systemic Embolism) in the Per-Protocol Population and in the Intention-to-Treat Population.

ROCKET AF (rivaroxaban)

P=0.01 for superiority

P>0.05 for superiority

# Rates of Bleeding Events.

## Table 3. Rates of Bleeding Events.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rivaroxaban (N=7111)</th>
<th>Warfarin (N=7125)</th>
<th>Hazard Ratio (95% CI)†</th>
<th>P Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events no. (%)</td>
<td>Event Rate no./100 patient-yr</td>
<td>Events no. (%)</td>
<td>Event Rate no./100 patient-yr</td>
</tr>
<tr>
<td>Principal safety end point: major and nonmajor clinically relevant bleeding§</td>
<td>1475 (20.7)</td>
<td>14.9</td>
<td>1449 (20.3)</td>
<td>14.5</td>
</tr>
<tr>
<td>Major bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>395 (5.6)</td>
<td>3.6</td>
<td>386 (5.4)</td>
<td>3.4</td>
</tr>
<tr>
<td>Decrease in hemoglobin ≥2 g/dl</td>
<td>305 (4.3)</td>
<td>2.8</td>
<td>254 (3.6)</td>
<td>2.3</td>
</tr>
<tr>
<td>Transfusion</td>
<td>183 (2.6)</td>
<td>1.6</td>
<td>149 (2.1)</td>
<td>1.3</td>
</tr>
<tr>
<td>Critical bleeding¶</td>
<td>91 (1.3)</td>
<td>0.8</td>
<td>133 (1.9)</td>
<td>1.2</td>
</tr>
<tr>
<td>Fatal bleeding</td>
<td>27 (0.4)</td>
<td>0.2</td>
<td>55 (0.8)</td>
<td>0.5</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>55 (0.8)</td>
<td>0.5</td>
<td>84 (1.2)</td>
<td>0.7</td>
</tr>
<tr>
<td>Nonmajor clinically relevant bleeding</td>
<td>1185 (16.7)</td>
<td>11.8</td>
<td>1151 (16.2)</td>
<td>11.4</td>
</tr>
</tbody>
</table>

* All analyses of rates of bleeding are based on the first event in the safety population during treatment.
† Hazard ratios are for the rivaroxaban group as compared with the warfarin group and were calculated with the use of Cox proportional-hazards models with the study group as a covariate.
‡ Two-sided P values are for superiority in the rivaroxaban group as compared with the warfarin group.
§ Minimal bleeding events were not included in the principal safety end point.
¶ Bleeding events were considered to be critical if they occurred in intracranial, intraspinal, intraocular, pericardial, intraarticular, intramuscular (with compartment syndrome), or retroperitoneal sites.

Apixaban
(Eliquis)

- Direct factor XA inhibitor (same mechanism as rivaroxaban)
- Recently approved in US
- BID dosing
- Rare side effects
- Data appears stronger than rivaroxaban
Aristotle trial
apixaban

• 18,201 patients
  – Atrial fibrillation
  – Additional risk factor for stroke
• Randomized to
  – Warfarin v.
  – Apixaban 5 mg BID
• Primary outcome stroke or systemic embolism
Kaplan–Meier Curves for the Primary Efficacy and Safety Outcomes.

ARISTOTLE
(apixaban)

Bleeding Outcomes and Net Clinical Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Apixaban Group (N=9088)</th>
<th>Warfarin Group (N=9052)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with Event no.</td>
<td>Event Rate %/yr</td>
<td>Patients with Event no.</td>
<td>Event Rate %/yr</td>
<td></td>
</tr>
<tr>
<td>Primary safety outcome: ISTH major bleeding†</td>
<td>327</td>
<td>2.13</td>
<td>462</td>
<td>3.09</td>
</tr>
<tr>
<td>Intracranial</td>
<td>52</td>
<td>0.33</td>
<td>122</td>
<td>0.80</td>
</tr>
<tr>
<td>Other location</td>
<td>275</td>
<td>1.79</td>
<td>340</td>
<td>2.27</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>105</td>
<td>0.76</td>
<td>119</td>
<td>0.86</td>
</tr>
<tr>
<td>Major or clinically relevant nonmajor bleeding</td>
<td>613</td>
<td>4.07</td>
<td>877</td>
<td>6.01</td>
</tr>
<tr>
<td>GUSTO severe bleeding</td>
<td>80</td>
<td>0.52</td>
<td>172</td>
<td>1.13</td>
</tr>
<tr>
<td>GUSTO moderate or severe bleeding</td>
<td>199</td>
<td>1.29</td>
<td>328</td>
<td>2.18</td>
</tr>
<tr>
<td>TIMI major bleeding</td>
<td>148</td>
<td>0.96</td>
<td>256</td>
<td>1.69</td>
</tr>
<tr>
<td>TIMI major or minor bleeding</td>
<td>239</td>
<td>1.55</td>
<td>370</td>
<td>2.46</td>
</tr>
<tr>
<td>Any bleeding</td>
<td>2356</td>
<td>18.1</td>
<td>3060</td>
<td>25.8</td>
</tr>
</tbody>
</table>

Net clinical outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Apixaban Group (N=9088)</th>
<th>Event Rate %/yr</th>
<th>Warfarin Group (N=9052)</th>
<th>Event Rate %/yr</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke, systemic embolism, or major bleeding</td>
<td>521</td>
<td>3.17</td>
<td>666</td>
<td>4.11</td>
<td>0.77 (0.69-0.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke, systemic embolism, major bleeding, or death from any cause</td>
<td>1009</td>
<td>6.13</td>
<td>1168</td>
<td>7.20</td>
<td>0.85 (0.78-0.92)</td>
<td>&lt;0.001</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 in the hierarchical sequence preserving a type I error.
Novel anticoagulants

- I have generally continued patients on warfarin unless
  - They have especially labile INRs
  - Express a desire to change
- More difficult to manage at time of other procedure (i.e. afib ablation)
- No specific antidote
New anticoagulants

• Appear to have an efficacy similar to warfarin
  – With similar to lower bleeding risks
• Much more expensive
  – But when cost of INR monitoring is included, cost difference narrows
  – Some insurance companies will only cover a new anticoagulant if warfarin is contraindicated
• Quick onset and offset, so that no bridging for procedures is required
  – But likely not safe to continue through procedures, as warfarin is for afib ablation, PPM placement, etc.
New anticoagulants

• Distinguishing between the novel anticoagulants is difficult
• Now we have too many choices?
• Hopefully best choices will become clear as time goes forward
Anticoagulation in the elderly

• For the elderly patient with afib, the decision to anticoagulate can be especially difficult
  – Benefit in terms of stroke reduction increases with age
  – Risk of bleeding, falls, etc. also increase

• This should be a highly individualized decision
  – Patient characteristics
  – Patient input into the decision
Atrial Fibrillation
symptom control

• Medications
  – Nodal slowing agents: Beta blockers, calcium channel blockers
  – Anti-arrhythmics: flecainide, propafenone, sotalol, dronedarone, dofetilide, amiodarone

• Cardioversion

• Permanent pacemaker
Indications for catheter ablation of atrial fibrillation

- Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication
- In rare clinical situations, it may be appropriate to perform AF ablation as first line therapy.
- Selected symptomatic patients with heart failure and/or reduced ejection fraction.
- The presence of a left atrial thrombus is a contraindication to catheter ablation of AF.
## Patient Selection for Ablation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Highly symptomatic</th>
<th>Minimally symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I and III drugs failed</td>
<td>≥1</td>
<td>0</td>
</tr>
<tr>
<td>AF type</td>
<td>Paroxysmal</td>
<td>Long-standing persistant</td>
</tr>
<tr>
<td>Age</td>
<td>Younger (&lt;70 years)</td>
<td>Older (≥70 years)</td>
</tr>
<tr>
<td>LA size</td>
<td>Smaller (&lt;5.0 cm)</td>
<td>Larger (≥5.0 cm)</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>Normal</td>
<td>Reduced</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Other cardiac disease</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Obesity</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Prior stroke/TIA</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Atrial Fibrillation is a Complex Arrhythmia
Schematic of Common Lesion Sets Employed in AF Ablation
Pre-Procedure CT with Image Integration
PV ablation
Started
Ablations at LPV-LAA ridge
LPV ablation completed
PV Mapping with Circular Multielectrode Catheter
LSPV Isolation

Pre

Post-Circle

Final
## Current Efficacy of AF Ablation

<table>
<thead>
<tr>
<th>Success:</th>
<th>Single Procedure</th>
<th>Multiple Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal patient:</td>
<td>70% - 80%</td>
<td>80% - 90%</td>
</tr>
<tr>
<td>Less optimal patient:</td>
<td>50% - 70%</td>
<td>70% - 80%</td>
</tr>
<tr>
<td>Poor candidate:</td>
<td>≤ 40%</td>
<td>40% - 60%</td>
</tr>
</tbody>
</table>
Cryoballoon ablation

- Alternative to radiofrequency energy
- Utilizes an over-the-wire balloon to occlude the pulmonary vein
  - Then cryoablate (freeze) the antrum of the vein to achieve conduction block
- Technically easier
- Faster
- Fewer complications
- Much less experience compared to radiofrequency energy
- We offer the cryoballoon procedure for patients with paroxysmal afib without prior ablation
Cryoballoon Technique
Why close the left atrial appendage?

- Atrial fibrillation is a strong risk factor for stroke
- Presumably, this relates to thrombus in the heart
  - Chiefly in the left atrial appendage
- Thus, closing the left atrial appendage should reduce the risk of stroke
History of Suture Closure

1947
Resection of the Left Auricular Appendix
A Prophylaxis for Recurrent Arterial Emboli
JOHN L. MADDEN, M.D.
Department of Surgery, Long Island College of Medicine, Kings County Hospital, Brooklyn, NY

1985
USE OF THE SURGICAL STAPLER TO OBLITERATE THE LEFT ATRIAL APPENDAGE
Laurence H. Coffin, M.D., F.A.C.S., Burlington, VT

2000
THE SURGICAL TREATMENT OF ATRIAL FIBRILLATION
IV. SURGICAL TECHNIQUE
JAMES L. COX, MD, St. Louis, Mo.
From the Division of Cardiothoracic Surgery, Department of Surgery, Washington University School of Medicine, Barnes Hospital, St. Louis, Mo.
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2011
ACC/AHA/ESC PRACTICE GUIDELINES—FULL TEXT
ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation

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, Krzysztof Bartus, and Steven J. Yakubov
Circ Cardiovasc Interventions published online May 16, 2010;
DOI: 10.1161/CIRCINTERVENTIONS.109.914978
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Feasibility of closed-chest ligation of the left atrial appendage in humans
Krzysztof Bartus, MD, PhD,1 Jacob Bednarek, MD, PhD,2,3 Jacek Myc, MD, Boguslaw Kapelało, MD,2,3 Jerzy Sadowski, MD, PhD,2,3 Jacek Latawiec, MD,2,4 Steven J. Yakubov, MD,5
Randall J. Lee, MD, PhD,6,7

Resection of the Left Atrial Appendage Using an Automatic Stapler
WILLIAM P. LONGMIRE, JR., M.D., JOHN M. BEAL, M.D., and WILLIAM H. LEAKE, M.D.
Los Angeles, California

Ligation of the Left Atrial Appendage Using an Automatic Stapler
WJ DeSena, S Tam, LI Cohn
Division of Cardiac Surgery, Brigham & Women’s Hospital, Boston, MA

Thoracoscopic Extracardiac Obliteration of the Left Atrial Appendage for Stroke Risk Reduction in Atrial Fibrillation
Joseph L. Blackshear, MD, W. Dudley Johnson, MD, John A. Odel, MD, Vickie S. Baker, RN, Mary Howard, RN, I. Lady Pears, MS, Christopher Stone, MD, Douglas L. Fisher, MD, Harrell V. Schiff, MD
Jacksonville, Florida, Milwaukee, Wisconsin, Minot, North Dakota, and Rochester, Minnesota
Percutaneous closure

- Stand alone open closure is not done
- Several potential percutaneous devices being developed/tested
- Major systems are Lariat and Watchman
- Watchman has been in development for 10 years
  - Involves placement of a covered cage in the appendage
Watchman data

- Endovascular “cage” placed in LA via transseptal puncture
- Occludes the left atrium and stimulates endothelialization
- Protect AF study
  - 707 patients with afib and CHADS2>=1 randomized 2:1 to Watchman v. continued warfarin
  - Warfarin continued for 45 days in watchman arm, then clopidogrel for 4.5 months, then lifelong ASA
- Not yet FDA approved
Kaplan-Meier curves of the primary efficacy end point.

Kaplan-Meier curves of the primary safety end point.

Lariat left atrial appendage closure

Bartus 2013, JACC 62:108
Figure 4   TEE Guidance for the Closure of the LAA  

(A) Transesophageal echocardiography (TEE) imaging of the LA and LAA at baseline  

(B) During the placement of the balloon at the orifice of the LAA. The balloon is used to define the orifice of the L...
Criteria for Lariat

- atrial fibrillation
- a CHADS2 score of 2 or higher
- contraindication to warfarin.
- **No prior chest surgery**
- not being offered to patients who just want to get off warfarin (or the equivalent)
PLACE Clinical Results

In a single center, non-randomized study (PLACE II)*, 85 patients underwent closure of their left atrial appendage using the LARIAT® Suture Delivery Device. Patients were followed at 1 day, 30 days, 90 days and 1 year with transesophageal echocardiography to determine closure quality. The results were as follows:

<table>
<thead>
<tr>
<th></th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td><strong>Intent-to-Treat</strong></td>
<td>85/89 (96%)</td>
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<tr>
<td><strong>Adverse Events</strong></td>
<td>3/89 (3.3%)**</td>
</tr>
<tr>
<td>(defined as access related or device failure)</td>
<td>Access 3/89 (3.3%)</td>
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<tr>
<td></td>
<td>Device 0/89 (0.0%)</td>
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<tr>
<td><strong>Closure</strong></td>
<td>1 day 81/85 (95%)</td>
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<tr>
<td>(defined as ≤ 1mm residual flow)</td>
<td>30 day 81/85 (95%)</td>
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<td></td>
<td>90 day 77/81 (95%)</td>
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<tr>
<td></td>
<td>1 year 65/66 (98%)</td>
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</table>

Bartus 2013, JACC 62:108
• How early to consider Afib ablation?
  – CABANA trial of medication v. ablation

• Management of novel anticoagulants at time of Afib ablation
  – Safe to continue novel anticoagulants without interruption through afib ablation?
    • VENTURE trial

• Pharmacogenetically directed treatment of afib
  • GENETIC-AF trial
Summary

• CHADS2, CHADSVASc, HASBLED tools are easy to use to aid in decision to anticoagulate
• Choices in anticoagulation are growing, and decisions should be made on an individual basis
• Left atrial appendage closure is coming!
• Proper assessment of symptoms is crucial for tailored treatment of afib
• There are lots of treatment options for symptom control in afib
Thanks!

Charles Henrikson, MD
Director, Electrophysiology Service
henrikso@ohsu.edu
503 494 7400
Atrial Fibrillation
new diagnosis

- May be managed as an outpatient
  - Often picked up incidentally
- Full assessment of symptoms
- Echocardiogram
  - Ejection fraction
  - Valvular abnormalities
  - Left atrial size
- Holter monitor
  - Afib burden
  - Range of ventricular rates

- Treatment
  - Start warfarin if appropriate
  - Nodal slowing agent if ventricular rate is elevated
- Referral to cardiology
  - Antiarrhythmic medications
  - Cardioversion
  - Permanent pacemaker
  - Radiofrequency ablation
Atrial fibrillation chronic management

• May be managed chronically by primary care provider
• Decision: Rhythm control v. rate control
• Warfarin or equivalent if indicated
• Nodal slowing agent if indicated
• Echocardiogram every several years
  – Ejection fraction
  – Left atrial size
Outline

• Introduction
• Natural history of afib and stroke
• SPAF studies
• Current risk stratification
  – CHADS
  – CHADS-VASc
  – HAS-BLED
• New oral anticoagulants
  – Dabigatran
  – Rivaroxaban
  – Apixaban
• Afib management and ablation
• Left atrial appendage closure
<table>
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<tr>
<th>SPAF</th>
<th>Comparison</th>
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<th>Source</th>
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<td>aspirin vs. placebo</td>
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<td><em>NEJM</em> 1990</td>
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<td>SPAF II</td>
<td>warfarin vs. aspirin</td>
<td>1100</td>
<td><em>Lancet</em> 1994</td>
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<td>SPAF III</td>
<td>warfarin vs. low-dose, warfarin + aspirin</td>
<td>1044</td>
<td><em>Lancet</em> 1996</td>
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Relative Risk of the Primary Outcome of Stroke or Systemic Embolism with Dabigatran versus Warfarin, According to Subgroup.

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<th>Subgroup</th>
<th>Patients total no.</th>
<th>Dabigatran 110 mg % per yr</th>
<th>Warfarin 150 mg % per yr</th>
<th>Hazard Ratio with Dabigatran, 110 mg (95% CI)</th>
<th>Hazard Ratio with Dabigatran, 150 mg (95% CI)</th>
<th>P Value for Interaction</th>
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</table>

Cumulative Rates of the Primary End Point (Stroke or Systemic Embolism) in the Per-Protocol Population and in the Intention-to-Treat Population.

ROCKET AF (rivaroxaban)

P=0.01 for superiority

P>0.05 for superiority

Cumulative Rates of the Primary End Point during Treatment and after Discontinuation in the Intention-to-Treat Population.

### Table 3. Rates of Bleeding Events.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rivaroxaban (N=7111)</th>
<th>Warfarin (N=7125)</th>
<th>Hazard Ratio (95% CI) †</th>
<th>P Value ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events no. (%)</td>
<td>Event Rate no./100 patient-yr</td>
<td>Events no. (%)</td>
<td>Event Rate no./100 patient-yr</td>
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<tr>
<td>Principal safety end point: major and nonmajor clinically relevant bleeding§</td>
<td>1475 (20.7)</td>
<td>14.9</td>
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<tr>
<td>Major bleeding</td>
<td></td>
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<td>Any</td>
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<td>Decrease in hemoglobin ≥2 g/dl</td>
<td>305 (4.3)</td>
<td>2.8</td>
<td>254 (3.6)</td>
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<td>Transfusion</td>
<td>183 (2.6)</td>
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<td>149 (2.1)</td>
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<td>Critical bleeding¶</td>
<td>91 (1.3)</td>
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<td>133 (1.9)</td>
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<td>Fatal bleeding</td>
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<td>0.2</td>
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<td>1185 (16.7)</td>
<td>11.8</td>
<td>1151 (16.2)</td>
<td>11.4</td>
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</table>

* All analyses of rates of bleeding are based on the first event in the safety population during treatment.
† Hazard ratios are for the rivaroxaban group as compared with the warfarin group and were calculated with the use of Cox proportional-hazards models with the study group as a covariate.
‡ Two-sided P values are for superiority in the rivaroxaban group as compared with the warfarin group.
§ Minimal bleeding events were not included in the principal safety end point.
¶ Bleeding events were considered to be critical if they occurred in intracranial, intraspinal, intraocular, pericardial, intraarticular, intramuscular (with compartment syndrome), or retroperitoneal sites.

Cumulative Rates of the Primary End Point during Treatment and after Discontinuation in the Intention-to-Treat Population.

![Graph showing cumulative event rates with data points for Rivaroxaban and Warfarin over days since drug discontinuation.]

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<th>Warfarin</th>
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### Risks of AF Ablation

**HRS Consensus Guide**

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<th>Complication Type</th>
<th>Rate</th>
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<tr>
<td>Major Complication Rates:</td>
<td>2% - 12%</td>
</tr>
<tr>
<td>Left atrial flutter:</td>
<td>5%</td>
</tr>
<tr>
<td>Vascular / access related:</td>
<td>1% - 5%</td>
</tr>
<tr>
<td>Cardiac tamponade:</td>
<td>0.5% - 3%</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.5% - 2%</td>
</tr>
<tr>
<td>PV stenosis:</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Phrenic nerve injury:</td>
<td>&lt; 0.5%</td>
</tr>
<tr>
<td>Esophageal perforation:</td>
<td>&lt; 0.2%</td>
</tr>
<tr>
<td>Death:</td>
<td>&lt; 0.1%</td>
</tr>
</tbody>
</table>

Calkins HR 2012, 9:632