Left Atrial Appendage Closure: The Good, The Bad and The Ugly

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Disclosures – Modest

• Advisory Board / Steering Committee
  – Biosense-Webster
  – Medtronic
  – Abbot EP

• Research
  – St. Jude
  – Biosense-Webster
  – Medtronic
  – Biotronik
  – Boston Scientific
The Problem:
**AF Increases Mortality/Morbidity:CVA Driven**
- Odds ratio for *bedridden state* after CVA due to AF = 2.23 (P < 0.0005) than stroke from any other cause
  (No Difference Between Paroxysmal vs Persistent)
- AF increases RR of *cognitive impairment* by 40%
- AF increases RR for *Dementia* by 38%
- **Risk of Stroke/Yr > 2%** (CHADS₂ or CHA₂DS₂VASc ≥ 2) without systemic anticoagulation (dementia and stroke risk still increased for CHADS 0 patients).
- 30-50% of AF pts have HasBled Score ≥ 3: Denotes 3.74 Bleeds/100 Pt Years
- Poor TTR with Warfarin results in greater risk of Emboli (low INR) and Dementia (high INR)

(How Do We Resolve Risk of Bleed vs. CVA?)

The Good News:
**Most Thrombi Come From the Left Atrial Appendage Which Can Be Closed**

Approximately 90% of LA clots come from the LAA
Variety of Closure Devices: External

- Aegis Intrapericardial Ligation
- Lariat
- Atriclip
- Tiger Paw II

Variety of Closure Devices: Internal

- Watchman
- Occlutech: LAA occluder
- The Transcatheter Patch
- Lifetech: LAmbre
- The Wavecrest From Coherex Medical
- Cardia Ultrasert Laa Occluder
U.S.: Watchman Device or Surgical Atriclip

**Stroke, systemic embolism, and cardiovascular mortality for Watchman, novel anticoagulants, and warfarin**

<table>
<thead>
<tr>
<th>Study</th>
<th>Stroke &amp; Systemic Embolism</th>
<th>Cardiovascular Mortality</th>
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<tr>
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<td>Watchman</td>
<td>Warfarin</td>
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<td>1065 pt y23</td>
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<td></td>
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<td></td>
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<td>1.8</td>
</tr>
</tbody>
</table>

Whisenant, et al: Intervent Cardiol Clinic 2014
Prevail

- Designed to address low Chad score of Protect AF and safety profile in experienced vs. inexperienced operators
- Randomized 407 pts Chads2 of ≥ 2 to Watchman or Warfarin in 2:1 fashion

Safety events within 7 days of the procedure decreased from the first half of PROTECT-AF (10.0 %) to Prevail (4.2%)

Prevail: 38.8 % of patients at new sites and 39.1 % of procedures being performed by new operators

CVA outcome underpowered

Feldmann et al; Current Cardiology Rep 2015

LAA Closure: The Bad News
Post implant management

Anticoagulation
- Warfarin + ASA for 45 days
- Switch to ASA and clopidogrel out to 6 months
- Then ASA alone indefinitely

Post implant TEE
- At 45 days, 6 & 12 months
- Screen leak or thrombus
- Peri-device leak > 5 mm is considered significant

Regulatory Requirements:
1. Shared decision making
2. CHADS2 ≥ 2 or CHA2DS2Vasc ≥ 3
3. Training and volume requirements
4. National Registry

LAA Closure: The Ugly
Leaks and Thrombi and Complications

Large Leak (Permanent Anticoagulation)

Embolized Amplatzer

Thrombi
- Occurrence 4%
- Late reports (3 yrs)
- Incomplete endothelialization

Stroke in AF patients

- People with AF have 5 times the risk of stroke compared to people without AF
- Stroke is more severe for patients with AF, as they have a 70% chance of death or permanent disability
- The economic burden of stroke will continue to rise globally as the incidence of stroke increases

2. Tu HT et al, Cerebrovascular Disease. 2010;30(4):389-95
Cardiac Pacing Milestones

- **External Pacemaker**
- **Implantable Pacemaker**
- **Rate Responsive Pacemaker**
- **MRI Conditional Pacemaker**
- **Intracardiac Pacemaker**

<table>
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<tr>
<th>Year</th>
<th>Device Type</th>
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<tr>
<td>1958</td>
<td>External Pacemaker</td>
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<tr>
<td>1960</td>
<td>Implantable Pacemaker</td>
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<tr>
<td>1986</td>
<td>Rate Responsive Pacemaker</td>
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<tr>
<td>2011</td>
<td>MRI Conditional Pacemaker</td>
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<tr>
<td>Today</td>
<td>Intracardiac Pacemaker</td>
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</table>

**Micra Pacing Capsule**

**Size**
- Volume: 0.8 cc
- Length: 25.9 mm
- Width: 20 Fr

**Battery**
- 12+ years estimated average longevity

**Capabilities**
- Pacing Mode: VVIR
- Bipolar sensing
- MRI SureScan™, allowing 1.5 T or 3 T full body MRI scans
- Capture Management™
- Rate Response
- Diagnostics: battery status, threshold, impedance, % paced
- Device can be manually deactivated and automatically deactivates at EOS

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New Opportunities To:

Reduce Chronic Complications Associated With Traditional Pacing Technology

Pocket Related Complications
4-8% at 5 years with traditional technology\(^1,2\)
- Infection
- Hematoma
- Erosion
- Pain

Lead Related Complications
5-11% at 5 years with traditional technology\(^1,2\)
- Fractures
- Insulation breaches
- Venous thrombosis and obstruction
- Tricuspid regurgitation

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Micra Procedure

![Micra Delivery System, Introducer and Dilator, Guide Wire, Needle](image)
Test fixation: Pull and Hold-Test

Fixation requirement:
• Ensure at least 2 tines are engaged in myocardium
The Micra TPS Global Clinical Trial

**Study Design:**
- Prospective, non-randomized, single-arm, multi-site, FDA IDE study
- Pre-defined historical control group for comparison †
  - 2667 patients from 6 trials of commercially available technology
- 725 patients, 94 implanters, 56 centers, 19 countries, 5 continents
  - North America, Europe, Asia, Australia, Africa
- VVIR patients: Class I or II guideline indication for de novo ventricular pacing with no restriction by comorbidity (e.g. COPD)

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**Baseline Characteristics**

**Micra Patients Older, More Comorbidities**

<table>
<thead>
<tr>
<th></th>
<th>Micra</th>
<th>Historical Control</th>
<th>p-value*</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>75.9 ± 10.9</td>
<td>71.1 ± 12.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>58.8%</td>
<td>55.1%</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>78.6%</td>
<td>67.2%</td>
<td>&lt;0.001</td>
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<tr>
<td>AF</td>
<td>72.6%</td>
<td>36.6%</td>
<td>&lt;0.001</td>
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<tr>
<td>Valvular Disease</td>
<td>42.2%</td>
<td>19.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>28.6%</td>
<td>21.9%†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAD</td>
<td>28.0%</td>
<td>38.4%</td>
<td>&lt;0.001</td>
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<tr>
<td>CHF</td>
<td>17.0%</td>
<td>15.0%</td>
<td>0.20</td>
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<tr>
<td>COPD</td>
<td>12.4%</td>
<td>7.2%†</td>
<td>0.001</td>
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<tr>
<td>Vascular Disease</td>
<td>7.3%</td>
<td>10.1%</td>
<td>0.032</td>
</tr>
</tbody>
</table>

†Data parameter not collected across all trials.
High Implant Success Rate

- 99.2% implant success (719 of 725 attempts) with 94 implanters

- Median implant time was 28 minutes introducer in to introducer out
  - 22 min after 1st 10 implants

51% Fewer Major Complications With Micra Vs Transvenous Pacemakers

To adjust for differences in patient populations, propensity matching to a subset of the historical control confirmed a reduction in major complications with Micra (HR: 0.46; 95% CI: 0.28 to 0.74).
Thank You!

Unanswered Questions

• Safety and efficacy of Epicardial vs. OAC
• Safety and efficacy of Endo vs. Epi
• Transition of Endocardial Closure with NOACs.
• Safety and efficacy of LAA occlusion in pts with contraindications to warfarin (ASAP Registry)
• 90% of the LA thrombi found in AF stroke patients are in the LAA, but LA thrombi are found in only 15-20%.
• Some patients will have embolic stroke from other sources.