Left Atrial Appendage Closure for Atrial Fibrillation

2015 UPDATE

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Disclosures

- Former proctor: SentreHEART
- Discussion may include the use of non-FDA approved devices or off-label use of devices.
Objectives

- Review the scientific evidence that supports LAA closure as a stroke prevention strategy in patients with non-valvular atrial fibrillation
- Discuss the devices available in the US in 2015
- Discuss the patient selection process
Stroke in the US

- 4th leading cause of death; leading cause of disability (38.6 billion in 09’)
- Lifetime risk: 1 in 5 women; 1 in 6 men
- 87% ischemic
- 23.5% due to AF (∼200,000) in pts >80 years
- Underestimated in asymptomatic AF
- AF increases risk of stroke 5-fold all ages; risk of AF, stroke and bleeding all increase with age
- 91-98% LAA involvement
- 40% of AF pts have a contraindication to anticoagulation

Right: 76 y old with AF (increased volume, >5 branches, > 40 twigs and no fine structures)

AHA Heart Disease and Stroke Statistics 2014 Circ 2013:129:e28-e292
Class IIb

1. Surgical excision of the LAA may be considered in patients undergoing cardiac surgery. (*Level of Evidence: C*)
Transcatheter Options
For the Patient Who can Tolerate Warfarin…
WATCHMAN

First implanted in 2002

CE Mark in 2005; FDA approved 2015
Protect AF Trial

- Non-valvular AF, CHADS$_2$ score $\geq 1$, randomized 2:1 WATCHMAN or warfarin

- Endpoints: stroke, CV death, systemic embolism and safety (bleeding, procedural complications effusion/stroke/embolization)

- Warfarin 45 days, ASA + clopidogrel for 4.5 m, then aspirin only

- 707 pts recruited (Watchman 463, control 244)

- Mean f/u 18 +/- 10 pt. months
Protect AF Trial

Primary Efficacy


3% vs 4.9% per year (Not Inferior)
Protect AF Trial

5.5% vs 3.6% per year

Primary Safety
Protect AF Trial

Primary Efficacy

Stroke

All-Cause Mortality

Landmark Analyses

PREVAIL Trial

**FIGURE 2** Kaplan-Meier Curve: Freedom From First Primary Endpoint (Intention-to-Treat)

Primary efficacy rates for Watchman (solid line) versus warfarin (dotted line) in the intention-to-treat population show similarly high 18-month event-free rates.

## Device Safety

<table>
<thead>
<tr>
<th>Table 7: Comparison of Outcomes in Device Patients in PROTECT AF, CAP, and PREVAIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROTECT AF</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Implant success</td>
</tr>
<tr>
<td>All 7-day procedural complications</td>
</tr>
<tr>
<td>Pericardial effusion requiring surgery</td>
</tr>
<tr>
<td>Pericardial effusion with pericardiocentesis</td>
</tr>
<tr>
<td>Procedure-related strokes</td>
</tr>
<tr>
<td>Device embolization</td>
</tr>
</tbody>
</table>
FDA Approval - Watchman

- March 2015
- Non-valvular atrial fibrillation
- Increased risk of stroke based on CHADS$_2$ or CHA$_2$DS$_2$-VASc score
- Deemed by physician to be suitable for warfarin
- Appropriate rationale to seek alternative to warfarin taking into account the safety and efficacy of the device
Watchman
Post Procedure Therapy

- Aspirin 81-100mg + warfarin (INR 2-3) x 45 days
- TEE at 45 days
- If closed (<5mm residual flow):
  - aspirin 325mg + clopidogrel 75mg x 4.5 months
  - then aspirin 300-325mg daily indefinitely
### Recommendations for LAA closure/oclusion/excision

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.</td>
<td>IIb</td>
<td>B</td>
<td>115, 118</td>
</tr>
<tr>
<td>Surgical excision of the LAA may be considered in patients undergoing open heart surgery.</td>
<td>IIb</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

LAA = left atrial appendage.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>References.
Transcatheter Options
For the Patient Who Cannot Tolerate Warfarin...
LARIAT SentreHEART

FDA Approved – soft tissue closure 2012

Not with specific indication for stroke prevention
PLACE II
Permanent Ligation Approximation Closure and Exclusion

- Non-randomized, single center, observational study
- Objective: assess safety and efficacy or LAA closure
- Patients with non-valvular AF, CHADS$_2$ >1 & ineligible to warfarin
- A poor candidate for warfarin therapy (e.g., labile INR level, non-compliant, contraindicated) and/or a warfarin failure (i.e. TIA or stroke while on warfarin therapy)
- Dec 2009 to Dec 2010; n=119

Bartus K, et al. JACC 2012 Sep 28; S0735-1097
PLACE II: Closure Follow Up

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Complete ≤1mm</th>
<th>≤2mm</th>
<th>≤3mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Closure</td>
<td>85</td>
<td>82 (96%)</td>
<td>2 (3%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>1d Closure</td>
<td>85</td>
<td>Complete ≤1mm</td>
<td>81 (95%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤2mm</td>
<td>3 (4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤3mm</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>&gt;30d Closure</td>
<td>85</td>
<td>Complete ≤1mm</td>
<td>81 (95%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤2mm</td>
<td>3 (4%)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>≤3mm</td>
<td>1 (1%)</td>
<td></td>
</tr>
<tr>
<td>&gt;90d Closure</td>
<td>81</td>
<td>Complete ≤1mm</td>
<td>77 (95%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤2mm</td>
<td>3 (4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤3mm</td>
<td>1 (1%)</td>
<td></td>
</tr>
</tbody>
</table>

* 4 patients had 60d follow up versus 90d

1 year 98% <1mm
2% < 2mm
<table>
<thead>
<tr>
<th># of LARIAT cases</th>
<th>Serious Injury to cardiac / related structure</th>
<th>&gt;2 PRBC in 2 days post Organs / structure requiring interven.</th>
<th>Fatal</th>
<th>Pericarditis requiring hosp or surg tx</th>
<th>Hemothorax</th>
<th>Pneumothorax</th>
<th>Vascular injury requiring surg treatment, hospitalization, transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afzal$^1$</td>
<td>50</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>Han$^2$</td>
<td>68</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Miller$^3$</td>
<td>41</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>2.40%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Price$^4$</td>
<td>154</td>
<td>1.90%</td>
<td>8.40%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Massumi$^5$</td>
<td>20</td>
<td>5.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Stone$^6$</td>
<td>27</td>
<td>3.70%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>3.70%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Bartus 2013$^7$</td>
<td>89</td>
<td>2.20%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Bartus 2011$^8$</td>
<td>11</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
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<tr>
<td>Sievert$^9$</td>
<td>139</td>
<td>2.80%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.70%</td>
</tr>
<tr>
<td>Lakkireddy$^{10}$</td>
<td>69</td>
<td>1.40%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>1.40%</td>
</tr>
<tr>
<td>Pilliariset$^{11}$</td>
<td>259</td>
<td>2.60%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td><strong>0-7.3%</strong></td>
<td><strong>0-8.4%</strong></td>
<td><strong>0-5.0%</strong></td>
<td><strong>0.00%</strong></td>
<td><strong>0-3.7%</strong></td>
<td><strong>0.00%</strong></td>
<td><strong>0-1.4%</strong></td>
</tr>
<tr>
<td><strong>Wtd Avg</strong></td>
<td><strong>927</strong></td>
<td><strong>2.32%</strong></td>
<td><strong>0.45%</strong></td>
<td><strong>0.27%</strong></td>
<td><strong>0.33%</strong></td>
<td><strong>0.00%</strong></td>
<td><strong>0.11%</strong></td>
</tr>
</tbody>
</table>
Asap trial
ASA Plavix feasibility study with Watchman

- 150 pts with non-valvular a-fib, CHADS$_2$ score $\geq$ 1, ineligible for warfarin (93% due to bleed)
- Multicenter, prospective, non-randomized
- Endpoints: stroke, CV/unexplained death, systemic embolism
- Clopidogrel or ticlopidine for 6 months and lifelong aspirin
- Mean f/u 14.4 +/- 8.6 months

ASAP Trial
ASA Plavix feasibility study with Watchman

6 pts (4%) had thrombus seen by TEE (164 +/- 135 days post)

Only one associated with stroke (341 days post)

The 5 pts without stroke were treated conservatively (4 with 4 to 8 weeks of LMWH and 1 no treatment)
Patient and Device Selection

ICH
Life threatening bleeding
Stroke off OAC
Life threatening bleeding
High CHADS$_2$
High CHADS$_2$
High HASBLED
Alternative to OAC
CONCLUSIONS

- The data suggests that LAA closure is not inferior (and perhaps superior) to anticoagulation

- Efficacy, mortality and Quality of Life benefits

- LAA closure is an option for high-risk pts with AF who have contraindications/intolerance to long term anticoagulation

- Long term and more safety data needed with newer devices