Nonpharmacologic Stroke Prevention and Surgical/Hybrid Strategies for AF Ablation

Raul Weiss, MD
LAA Closure Devices for Stroke Prevention in Patient with Atrial Fibrillation

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Director Electrophysiology Fellowship Program
Professor of Medicine
The Ohio State University
Objectives

- Rationale for LAA Closure
- Pro and Cons of LAA closure surgically
- Pro and Cons of LAA closure percutaneously
- Summarize to you relevant and emerging data
Disclosures

- Educational and Research support from Boston Scientific, Medtronic, St Jude, Biotronik, Biosense Webster, Gene Dx, Cameron Health and Stereotaxis

- Advisory honoraria from PGx Health, Stereotaxis, Biosense Webster, Biotronik, Cameron Health and Boston Scientific

- Speaker honoraria from St Jude, Biotronik, Medtronic, Stereotaxis, Biosense Webster and Cameron Health

- I may be discussing FDA-approved devices for non approve FDA indication and Non FDA-approved device that are CE mark
“Our Most Lethal Human Attachment”
Embryology

- The trabecular LAA is the remnant of the original embryonic left atrium that develops during the third week of gestation.
- The main smooth walled left atrial cavity develops later and is formed from the outgrowth of the pulmonary veins.
LAA Closure Devices Already in the Guidelines

- The European Society of Cardiology (ESC) announced the inclusion of LAA closure devices in the revised "Guidelines for Management of Patients with Atrial Fibrillation."

- Recommendation was based on the expansive WATCHMAN LAA closure device clinical data, collected on more than 2,000 patients and exceeded the equivalent of 4,000 patient years of follow up across multiple studies.
History of LAA closure

- LAA obliteration was first suggested as an adjunct to mitral valvotomy before the advent of cardiopulmonary bypass 1949
- Surgical enthusiasm was high in the 80 and 90s
- Early 2000s saw the first percutaneous device
- 2010 large number of percutaneous devices and techniques are being tested
History: Number of left atrial appendage publications from 1948 to 2011

Anatomy
LAA Anatomy

- The 2-cm to 4-cm-long tubular LAA usually forms a narrow junction with the LA and angles downward from its origin.
- Significant heterogeneity among AF patients in LAA size, wall thickness, and morphology.
LAA Anatomy
Anatomy of the Normal Left Atrial Appendage
Left Atrial Appendage Measurements by Age Category and Sex

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Sex</th>
<th>Diameter, cm</th>
<th>Length, cm</th>
<th>Width, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>Male</td>
<td>0.80 ± 0.27</td>
<td>2.52 ± 0.73</td>
<td>1.38 ± 0.42</td>
</tr>
<tr>
<td>&lt;20</td>
<td>Female</td>
<td>0.86 ± 0.26</td>
<td>2.29 ± 0.53</td>
<td>1.38 ± 0.46</td>
</tr>
<tr>
<td>≥20</td>
<td>Male</td>
<td>1.16 ± 0.35</td>
<td>2.59 ± 0.66</td>
<td>1.83 ± 0.73</td>
</tr>
<tr>
<td>≥20</td>
<td>Female</td>
<td>1.07 ± 0.32</td>
<td>2.53 ± 0.78</td>
<td>1.66 ± 0.48</td>
</tr>
</tbody>
</table>
LAA Anatomy: Distribution of Number of Lobes

- 23% 3 lobes
- 54% 4 lobes
- 20% 1 lobe
- 3% 2 lobes

LAA Anatomy: Length as a Function of Age for Males and Female

A

Male

B

Female

Length LAA (cm)

Age (yr)
Orifice size of left atrial appendage (LAA) as a function of age for A, male subjects, and B, female subjects.

Diagram of a Left Atrial Appendage Shows lobes 1, 2, and 3.

Measurements of LAA in an Anatomic Specimen.

Function
Function

- Animal studies demonstrate that the LAA contains stretch receptors that mediate thirst
- Endocrine function is shown by a 40-fold higher concentration of atrial natriuretic peptide compared with other areas of the heart
- The LAA may have a role in the regulation of LA pressure–volume relationships in fluid homeostasis such that LAA occlusion may lead to altered LA compliance
Function II

- An underappreciated role of the LAA is as a trigger for recurrent AF after catheter ablation, as was seen in 27% of patients in a large review of 987 cases.
Surgical Techniques for LAA Occlusion

- **Exclusion**
  - Within the exclusion method are running or mattressed sutures, with and without felt pledgets. Specifically, the ligation occurs on the epicardial surface or more commonly, from the endocardial surface.

- **Excision**
  - The most common techniques within the excision method include a stapled excision or removal and oversew.
Epicardial suture exclusion

Endocardial suture exclusion

Stapled excision

Removal and Oversew

## Comparison of Surgical Left Atrial Appendage Closure Techniques

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Country</th>
<th>No. Studied</th>
<th>Method of Closure</th>
<th>Closure Success Rate, %</th>
<th>Effect of LAA Closure on Stroke Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson, 2000 [25]</td>
<td>USA</td>
<td>437</td>
<td>Excision</td>
<td>100</td>
<td>Positive</td>
</tr>
<tr>
<td>Katz, 2000 [30]</td>
<td>USA</td>
<td>50</td>
<td>Endocardial suture</td>
<td>64</td>
<td>None</td>
</tr>
<tr>
<td>Garcia-Fernandez, 2003 [31]</td>
<td>Spain</td>
<td>205</td>
<td>Endocardial suture</td>
<td>90</td>
<td>Positive</td>
</tr>
<tr>
<td>Bando, 2003 [38]</td>
<td>Japan</td>
<td>812</td>
<td>Endocardial suture</td>
<td>Not measured</td>
<td>Negative</td>
</tr>
<tr>
<td>Blackshear, 2003 [45]</td>
<td>USA</td>
<td>15</td>
<td>Thoracoscopic epicardial pursestring</td>
<td>93(^b)</td>
<td>Positive</td>
</tr>
<tr>
<td>Pennec, 2003 [40]</td>
<td>France</td>
<td>30</td>
<td>Endocardial</td>
<td>70–80</td>
<td>Negative</td>
</tr>
<tr>
<td>Schneider, 2005 [41]</td>
<td>Germany</td>
<td>6</td>
<td>Excision</td>
<td>100</td>
<td>Positive</td>
</tr>
<tr>
<td>Healey, 2005 [28]</td>
<td>Canada</td>
<td>77</td>
<td>Endocardial suture</td>
<td>17</td>
<td>Negative</td>
</tr>
<tr>
<td>Kanderian, 2008 [29]</td>
<td>USA</td>
<td>137</td>
<td>Epicardial suture</td>
<td>45</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stapler</td>
<td>72</td>
<td>Positive trend</td>
</tr>
<tr>
<td>Bakhtiari, 2008 [33]</td>
<td>Germany</td>
<td>259</td>
<td>Excision</td>
<td>73 (20% stapler)</td>
<td>Positive trend</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Suture exclusion</td>
<td>23</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stapler</td>
<td>0</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Clamp and epicardial suture</td>
<td>100(^b)</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Role in the Pathology of Thromboembolic Stroke
Watchman
Three trials of the WATCHMAN® Device have reached their primary endpoints; a fourth is ongoing

<table>
<thead>
<tr>
<th></th>
<th>PROTECT AF&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>CAP&lt;sup&gt;2&lt;/sup&gt;</th>
<th>ASAP&lt;sup&gt;3,4&lt;/sup&gt;</th>
<th>PREVAIL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control</strong></td>
<td>Patients able to take warfarin</td>
<td>Warfarin contraindicated patients</td>
<td>Patients able to take warfarin</td>
<td></td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>All stroke, systemic embolism and cardiovascular death</td>
<td>All stroke, systemic embolism and cardiovascular death</td>
<td>All stroke, systemic embolism, and cardiovascular death</td>
<td>All stroke, systemic embolism and cardiovascular death</td>
</tr>
<tr>
<td><strong>Mean age /CHADS</strong></td>
<td>72/2.2</td>
<td>74/2.4</td>
<td>72.4/2.8</td>
<td>ongoing</td>
</tr>
<tr>
<td><strong>Total Enrolled Subjects</strong></td>
<td>707 randomized&lt;sup&gt;1&lt;/sup&gt;, 93 pts rolled in&lt;sup&gt;2&lt;/sup&gt;</td>
<td>460</td>
<td>150</td>
<td>461</td>
</tr>
<tr>
<td><strong>Total Patients Implanted</strong></td>
<td>542&lt;sup&gt;2&lt;/sup&gt;</td>
<td>437</td>
<td>142</td>
<td></td>
</tr>
<tr>
<td><strong>Implantation Success</strong></td>
<td>89.5%&lt;sup&gt;2&lt;/sup&gt;</td>
<td>95.0%</td>
<td>94.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Warfarin discontinuation at 45 days</strong></td>
<td>86.6%</td>
<td>94.9%</td>
<td>No warfarin used</td>
<td></td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>Rate ratio 0.71 (0.35–1.64) [Hemorrhagic Stroke: 0.09 (0.00–0.45)]</td>
<td>Reduction in procedure related stroke vs PROTECT AF (&lt;i&gt;P&lt;/i&gt;=0.04)</td>
<td>Decreased rate of stroke by 77% vs. expected rate per CHADS&lt;sub&gt;2&lt;/sub&gt; Score</td>
<td></td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>HR 1.69 (1.01–3.19)</td>
<td>Reduction in pericardial effusions vs PROTECT AF (&lt;i&gt;P&lt;/i&gt;=0.02)</td>
<td>Pericardial effusion with tamponade=2.0% Major bleeding=2.7%</td>
<td></td>
</tr>
</tbody>
</table>

3. Sievert H. TCT 2011  
4. Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
The PROTECT AF trial demonstrated non-inferiority of the WATCHMAN® Device to warfarin in 707 randomized patients

- PROTECT AF was a prospective, randomized, multi-center trial which compared the WATCHMAN Device to warfarin for thromboembolic prophylaxis
- 707 patients were randomized to either the WATCHMAN Device or warfarin in a 2:1 device to therapy ratio; 93 roll-in patients

Patients who received the WATCHMAN Device had 45 days of post operative warfarin therapy to ensure endothelialization

- Transesophageal echocardiography was performed at 45 days, 6 months and 1 year to check for device placement, presence of thrombus and flow
- Patients received up to 5 years of biannual follow-up

<table>
<thead>
<tr>
<th>Baseline Risk Factors</th>
<th>WATCHMAN®</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHADS2</td>
<td>1</td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>36.1%</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>20.9%</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>9.8%</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>4.1%</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>2%</td>
</tr>
</tbody>
</table>

Average age for WATCHMAN® was 71.7 years ± 8.8 years

PROTECT AF
Primary Efficacy & Safety Endpoints

- 91% of patients had successful implantation
- 87% of implanted patients discontinued warfarin at 45 days
- 92% of implanted patients had LAA closure at 6 months
PROTECT AF
Clinical event rates at 1065 patient years

Overall, stroke was not significantly different between arms (HR 1.34 (0.60-4.29))

Following the periprocedural period, the rate of ischemic stroke with the WATCHMAN® Device was 1.3 per 100 patient years vs 1.6 with warfarin.
PROTECT AF
Ischemic and Hemorrhagic Stroke Rates

Rate of ischemic stroke over time

Rate of hemorrhagic stroke over time

Watchman
warfarin

Percent of patients
 Percent of patients
Both the WATCHMAN Device and warfarin patients experienced adverse events

The WATCHMAN Device events were concentrated around the time of the procedure

Warfarin events occurred at any time (not shown)

*From tests for differences across three groups (early PROTECT AF, late PROTECT AF, and CAP)
A continued access registry demonstrated ongoing improvement in the WATCHMAN® Device procedure implantation success

- A continued access registry (CAP) enrolled an additional 437 patients at 26 centers which had also participated in PROTECT AF

<table>
<thead>
<tr>
<th></th>
<th>PROTECT AF</th>
<th>CAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>72</td>
<td>74</td>
</tr>
<tr>
<td>Mean CHADS$_2$</td>
<td>2.2</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Pericardial effusion rates within 7 days of the procedure:

- Pericardial effusion was the most common adverse event in the WATCHMAN® Device group.
- Of patients experiencing pericardial effusion, 68% were treated with pericardiocentesis and 32% required surgical intervention.
- Rates of pericardial effusion declined at each center as experience with the procedure increased.

Procedure Related Safety Events

Rates of safety events within 7 days of procedure in PROTECT AF and CAP registry

- Of patients experiencing pericardial effusion in CAP, 90% were treated with pericardiocentesis and 10% required surgical intervention.


- Reduction of ~50% in pericardial effusion rates between studies.
- Procedure-related stroke reduced to 0.

Of patients experiencing pericardial effusion in CAP, 90% were treated with pericardiocentesis and 10% required surgical intervention.
The ASAP registry, a non-randomized feasibility study, was designed to determine if the WATCHMAN® Device is a safe and effective treatment for people unable to take warfarin.

- AF patients who are contraindicated or intolerant of warfarin have few options for thromboembolic prophylaxis.
- Patients may be treated with aspirin and/or clopidogrel; this treatment paradigm has a higher stroke risk than warfarin.

Hart RG et al. Stroke. 2004;35:948-951
ASAP Registry
ASAP enrolled 150 AF patients contraindicated for long-term warfarin therapy

- These patients had a history of hemorrhagic & bleeding tendencies or a hypersensitivity to warfarin
- 150 patients were enrolled at 4 European centers
- Average CHADS$_2$ of enrolled patients = 2.8
- Post procedure anti-platelet regimen
  - Clopidogrel through 6 months
  - Aspirin indefinitely
- Patients were followed for up to 1 year
  - Follow-up @ 3, 6, 12, 18 & 24 months
  - TEE at 3 and 12 months

Rate of Success with implantation in warfarin contraindicated patients

94.7% successfully implanted

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
ASAP Registry
Expected Stroke Rate

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
Expected, based on CHADS₂ Score

Observed rate in ASAP

77% Reduction

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
ASAP Registry
Efficacy Outcome vs. Expected

Ischemic Stroke Rate (%/pt-yr)

- **7.3%**
- **5.1%**
- **1.7%**

- **77% Reduction** Expected, based on CHADS² Score
- **67% Reduction** Expected, if Clopidogrel was used throughout follow-up
- **Observed rate in ASAP**
ASAP Registry
Efficacy Outcomes with Devices

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
Study Objective: To evaluate the long term embolic stroke rate of patients implanted with the WATCHMAN® left atrial appendage closure

Study Design: Prospective, multicenter

Primary Endpoint: Embolic stroke

Patient Population: n=66; Mean age=68.5±8 years; Mean CHADS2 score=1.8±1.1

Mean Follow Up: 73±25 months

Number of Sites: 8 (US and Germany)

Presented by: Peter B. Sick, MD,; ESC 2012
Ischemic Stroke

- 2 embolic strokes over 6 years of follow up*
- A 90% reduction when compared to CHADS₂ expected stroke rate

*One stroke at 2 months and one at 39 months in the setting of severe carotid disease

Sick, et al., WATCHMAN Pilot data; ESC 2012, Munich, Germany
Study Objective: Evaluate the PROtECT AF trial results using CHA$_2$DS$_2$VASc scores to better determine stroke risk

Study Design: PROTECT AF design used CHADS$_2$ scores. This analysis uses the same data replacing the CHADS$_2$ score with the CHA$_2$DS$_2$VASc score.

Primary Endpoint: Embolic stroke

Patient Population: n=463; Mean age=72; Mean CHADS$_2$ score=2.2, Mean CHA$_2$DS$_2$VASc = 3.5

Total Follow Up: 1500 patient years

Number of Sites: 59 in the United States and Europe

Presented by: Sven Mobius–Winkler,; ESC 2012
93% had CHA2DS2VASc score >2
Average CHA2DS2Vasc score: 3.5
Expected risk of stroke: 3%
Observed stroke rate: 2%
37.5% reduction compared to expected

Expected rate based on CHA2DS2VASc score
Observed rate
PREVAIL
A Second Randomized Study of the WATCHMAN® Device is Underway

• Prospective, multi-center, randomized (2:1) study comparing WATCHMAN to warfarin therapy (PREVAIL)

• Up to 50 sites in the U.S.

• 400 randomized and up to 75 roll-in patients
  ▪ Minimum 20% of patients from new sites
  ▪ Minimum 25% patients by new operators

• 1st Primary Endpoint (same as PROTECT AF)
  ▪ Ischemic stroke, hemorrhagic stroke, systemic embolism and cardiovascular/unexplained death

• 2nd Primary Endpoint
  ▪ Ischemic stroke and systemic embolism >7 days post randomization

• Timeline
  ▪ Final randomized patient enrolled June 2012
Adverse Event Comparison of Current Transcatheter Closure Devices

<table>
<thead>
<tr>
<th>Study</th>
<th>Device</th>
<th>Pts in Study (No.)</th>
<th>Age, Years (Mean ± SD)</th>
<th>Procedural Stroke No. (%)</th>
<th>Device Embolization No. (%)</th>
<th>Major Pericardial Effusion or Tamponade No. (%)</th>
<th>Bleeding No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial European experience</td>
<td>Amplatzer Cardiac</td>
<td>143</td>
<td>74 ± 9</td>
<td>3 (2)</td>
<td>2 (1)³</td>
<td>5 (4)</td>
<td>NR</td>
</tr>
<tr>
<td>PROTECT-AF [55]</td>
<td>Watchman</td>
<td>463</td>
<td>72 ± 9</td>
<td>5 (1)</td>
<td>3 (0.6)²</td>
<td>22 (5)</td>
<td>16 (4)</td>
</tr>
<tr>
<td>CAP Registry [39]</td>
<td>Watchman</td>
<td>460</td>
<td>74 ± 8</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>10 (2)</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

Device Intended Use

The AMPLATZER™ Cardiac Plug (ACP) is a percutaneous transcatheter device intended to prevent thrombus embolization from the left atrial appendage (LAA) in subjects who have nonvalvular atrial fibrillation.
Device Description

The ACP device is delivered transseptally via delivery sheath into the left atrium (LA) and to the LAA
Device Description

ACP Device Configurations

Eight device sizes (mm) (16, 18, 20, 22, 24, 26, 28, 30)

Disc Diameter 20 – 36 mm
Lobe Diameter  16 – 30 mm
Lobe Length     6.5 mm
Practical Differences Between LAACD

- Amplatzer Cardiac Plug: no oral anticoagulants routinely used and the long term dual antiplatelet therapy (DAT) is not required. Only initial DAT regimen (6 months of aspirin and 1 month of clopidogrel) is routinely prescribed.

- WATCHMAN filter: oral anticoagulants administered for at least 45 days with target INR of 2.0-3.0 and after its withdrawal long-term aspirin is recommended.
Overview of the LARIAT implantation technique
Percutaneous Left Atrial Appendage Suture Ligation Using the LARIAT Device in Patients With Atrial Fibrillation

Initial Clinical Experience

Krzysztof Bartus, MD, PhD,* Frederick T. Han, MD,† Jacek Bednarek, MD, PhD,‡
Jacek Myc, MD, PhD,* Boguslaw Kapelak, MD, PhD,* Jerzy Sadowski, MD, PhD,*
Jacek Lelakowski, MD, PhD,‡ Stanislaw Bartus, MD, PhD,* Steven J. Yakubov, MD,§
Randall J. Lee, MD, PhD†¶

Krakow, Poland; San Francisco, California, and Columbus, Ohio
Inclusion Criteria:

1) Age 18 years or older
2) Non-valvular AF
3) CHADS 1 or higher
4) Poor candidate or ineligible for warfarin therapy (labile international normalized ratio level, noncompliant, contraindicated) and/or a warfarin failure (i.e., transient ischemic attack or stroke while on warfarin therapy)
5) Life expectancy of at least 1 year

K Bartus et. Al. J Am Coll Cardiol 2012 in press
Exclusion Criteria:

1) History of pericarditis
2) History of cardiac surgery
3) Pectus excavatum
4) Recent myocardial infarction within 3 months
5) Prior embolic event within the last 30 days
6) New York Heart Association functional class IV heart failure symptoms
7) Left ventricular function 30%
8) History of thoracic radiation

K Bartus et Al. J Am Coll Cardiol 2012 in press
Exclusion Criteria Based on LAA Anatomy:

1) a LAA width 40 mm;

2) Superiorly oriented LAA with the LAA apex directed behind the pulmonary trunk

3) Bilobed LAA or multilobed LAA in which lobes were oriented in different planes exceeding 40 mm

4) Posteriorly rotated heart

K Bartus et. Al. J Am Coll Cardiol 2012 in press
Components for the Percutaneous LAA Ligation Procedure

A magnet guide wires
B endocath occlusion balloon
C suture delivery device

K Bartus et. Al. J Am Coll Cardiol 2012 in press
Baseline Characteristics (N=89)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intent-to-Treat Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>62 ± 10</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>51 (57%)</td>
</tr>
<tr>
<td>Female</td>
<td>38 (43%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>30 (34%)</td>
</tr>
<tr>
<td>Persistent</td>
<td>59 (66%)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>11 (12%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84 (94%)</td>
</tr>
<tr>
<td>Age ≥75 yrs</td>
<td>11 (12%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>9 (10%)</td>
</tr>
<tr>
<td>Stroke/transient ischemic attack while on OAC</td>
<td>22 (25%)</td>
</tr>
<tr>
<td>Failure/complication* while on OAC</td>
<td>12 (13%)</td>
</tr>
<tr>
<td>Contraindicated to OAC</td>
<td>5 (5.6%)</td>
</tr>
<tr>
<td>Labile INR</td>
<td>57 (64%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Left atrial appendage characteristics</td>
<td></td>
</tr>
<tr>
<td>Width, mm†</td>
<td>26 ± 7.4</td>
</tr>
<tr>
<td>Length, mm‡</td>
<td>32 ± 7.4</td>
</tr>
<tr>
<td>Number of lobes</td>
<td>2.0 ± 0.74</td>
</tr>
<tr>
<td>Pre-ligation medication</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>84 (94%)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Aspirin + clopidogrel</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

K Bartus et. Al. J Am Coll Cardiol 2012 in press
Fluoroscopic Guidance to Assist in the Closure of the LAA

K Bartus et. Al. J Am Coll Cardiol 2012 in press
The Procedure Involves 4 Basic Steps:

- 1) pericardial and transseptal access
- 2) placement of the endocardial magnet-tipped guidewire in the apex of the LAA with balloon identification of the LAA os
- 3) connection of the epicardial and endocardial magnet-tipped guidewires for stabilization of the LAA
- 4) snare capture of the LAA with closure confirmation and release of the pre-tied suture for LAA ligation

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Figure 6  Pericardial Access Approach The angle of access in the anterior-posterior view (AP) (A) and lateral view (B).

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Percutaneous Left Atrial Appendage Suture Ligation Using the LARIAT Device in Patients With Atrial Fibrillation: Initial Clinical Experience
Journal of the American College of Cardiology null 2012 null

http://dx.doi.org/10.1016/j.jacc.2012.06.046
Figure 2  3D CT Reconstruction  Cardiac 3-dimensional (3D) computed tomography (CT) reconstruction is used for determining the size, shape, and orientation of the left atrial appendage (LAA). The 3D CT reconstruction aids in the guidance of the pe...

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Figure 4  TEE Guidance for the Closure of the LAA  Transesophageal echocardiography (TEE) imaging of the LA and LAA at baseline (A) and during the placement of the balloon at the orifice of the LAA (B). The balloon is used to define the orifice...

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Flow Diagram of Patients Screened for LAA Exclusion

PATIENTS SCREENED
N=119

PATIENTS EXCLUDED
N=16 (13.4%)

- LAA Width ≥40mm
  N=8 (6.7%)
- Unsuitable AA Orientation
  N=8 (6.7%)

ELIGIBLE PATIENTS
N=103 (86.5%)

EXCLUDED AT TIME OF PROCEDURE
N=14 (13.6%)

- Presence of Adhesion
  N=3 (2.9%)
- Mobile Thrombus+
  N=11 (10.7%)

PATIENTS TO BE TREATED
N=89 (86.4%)

FAILURE TO TREAT
N=4 (4.5%)

SUCCESSFUL LAA CLOSURE
N=85 (95.5%)

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LAA Ligation Results (N=89)

<table>
<thead>
<tr>
<th>Successful ligation</th>
<th>85 (96%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>3 (3.3%)</td>
</tr>
<tr>
<td>Device related</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Access related</td>
<td>3 (3.3%)</td>
</tr>
<tr>
<td>Pericardial access</td>
<td>2 (2.2%)</td>
</tr>
<tr>
<td>Transseptal access</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Inability to complete ligation</td>
<td>1 (1.1%)</td>
</tr>
<tr>
<td>Pericardial adhesions in LAA sulcus</td>
<td></td>
</tr>
</tbody>
</table>

### End of procedure closure (n = 85)

<table>
<thead>
<tr>
<th>Complete or &lt;1-mm leak</th>
<th>82 (96%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2-mm leak</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>&lt;3-mm leak</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

### 1 day post procedure closure by TEE (n = 85)

<table>
<thead>
<tr>
<th>Complete or &lt;1-mm leak</th>
<th>81 (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2-mm leak</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>&lt;3-mm leak</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

### 30 days post procedure closure by TEE (n = 85)

<table>
<thead>
<tr>
<th>Complete or &lt;1-mm leak</th>
<th>81 (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2-mm leak</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>&lt;3-mm leak</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

### 90 days post procedure closure by TEE (n = 81)

<table>
<thead>
<tr>
<th>Complete or &lt;1-mm leak</th>
<th>77 (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2-mm leak</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>&lt;3-mm leak</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

### 1 year post procedure closure by TEE (n = 65)

<table>
<thead>
<tr>
<th>Complete or &lt;1-mm leak</th>
<th>64 (98%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2-mm leak</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

### Rhythm pre-ligation

- Sinus rhythm | 57 (64%)
- Atrial fibrillation | 29 (33%)
- Atrial flutter | 3 (3%)
- Not available | 0

### Rhythm post-ligation

- Sinus rhythm | 56 (63%)
- Atrial fibrillation | 30 (34%)
- Atrial flutter | 2 (2%)
- Not available* | 1 (1%)

**Procedural time, min**

| 45 (36-55) |

**Fluoroscopy time, min**

| 13.6 ± 6.5 |

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The Left Atrial Appendage, a Small, Blind-Ended Structure*: A Review of Its Echocardiographic Evaluation and Its Clinical Role


Figure Legend:

Top left, A: Example of a polylobed LAA with severe SEC and the corresponding pulsed Doppler of LAA flows. Top right, B: Second example of polylobed LAA. Bottom left, C: Example of an LAA ligated by the surgeon at the time of plasty of the mitral valve; the ligature is incomplete and there is still flow between the LAA and the LA cavity.
The Left Atrial Appendage, a Small, Blind-Ended Structure*: A Review of Its Echocardiographic Evaluation and Its Clinical Role


Figure Legend:
Example of LAA flow recording after spontaneous conversion to SR in a dog model.
The Left Atrial Appendage, a Small, Blind-Ended Structure*: A Review of Its Echocardiographic Evaluation and Its Clinical Role


Figure Legend:

Representation of LAA pulsed Doppler ECG recording in SR (left, A) and AF (right, B). The mitral inflow recorded in pulsed Doppler, the LV outflow tract flow, and the pulmonary vein flows are also presented on these two diagrams to illustrate their timing. e = passive LAA emptying flow; a = active LAA emptying flow; f = passive LAA emptying flow in AF; E = early diastolic mitral inflow; A = late-diastolic mitral inflow; S = systolic pulmonary venous flow; D = diastolic pulmonary venous flow; Arev = active reversal wave recorded in the pulmonary vein corresponding to the active contraction of the atrium.
Figure Legend:

Example of 2-D transthoracic assessment of the LAA and with the pulsed Doppler assessment of flows.