The Left Atrial Appendage & Closure Interventions

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Disclosures:
• None

Why the left atrial appendage topic?
Embryogenesis

- The only structure in the LA derived from the primitive atrium
- The rest are a part of PVs and are characterized by a smooth endocardium.
- The LAA is not just an embryologic remnant, but it play an important role:
  - Regulation of heart rate and fluid balance
  - Thromboembolic risk associated with AF
  - Triggering effect of atrial tachyarrhythmias

Thromboembolism Risk

Frequency & Sites of Thrombus Locations in Non-valvular AF

Appendage Obliteration to Reduce Stroke in Cardiac Surgical Patients With Atrial Fibrillation

Joseph L. Blackshear, MD, and John A. Sullivan, MD, FACC

Background: Left atrial appendage obliteration may be considered for the prevention of postoperative thromboembolic events when surgical failure is anticipated. The left atrial appendage was originally a temporary structure in the embryologic development of the heart.

Methods: The potential for left atrial appendage obliteration to prevent stroke in mechanically isolated, atrial fibrillation (AF) patients undergoing surgery was evaluated. Apparatus was necessary to isolate the left atrial appendage and could be used in the left atrium to facilitate treatment of AF patients with a temporary electrical isolating device.

Results: The incidence of stroke was reduced in patients with left atrial appendage obliteration.

Conclusion: Left atrial appendage obliteration is a strategy of potential for stroke prevention in patients with AF.

2014 ACC/AHA/HRS AF Guidelines

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCM, LVEF ≤ 40%</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>AF/flutter, stroke risk</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>AF/flutter, stroke risk</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>ECHOCG, TTE, TEE, or echocardiography</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Transesophageal echocardiography</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Transcranial Doppler ultrasound</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Warfarin</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>DOACs</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>ASA</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>ASA or warfarin</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>ASA or warfarin</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Warfarin or DOAC</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Warfarin or DOAC</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>ASA or warfarin</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>
LAA was responsible for arrhythmias in 27% of patients presenting for repeat ablation procedures.

LAA Morphology and Risk of Stroke

Does the Left Atrial Appendage Morphology Correlate With the Risk of Stroke in Patients With Atrial Fibrillation?

Results From a Multicenter Study

Luigi Di Biase, MD, Paolo Santangeli, MD, Matteo Ambrosioni, MD, PhD
Pierluigi Maestri, MD, SR, Salvatore Santoro, MD, PhD, Paolo Santamore, MD, PhD, Renato Prinetti, MD
Javier P. Sanchez, MD, Hong Liu, MD, Stefania Pietrantoni, MD, Luo Peng, MD
Mariano Ceravolo, Dr., MD, Giuseppe Carminati, MD, Luigi Di Biase, MD
Federico Cesaro, MD, Marco Seghieri, MD, Andrea Malavolta, MD
Ferruccio Franzosi, MD, Luigi Di Biase, MD, PhD, Paolo Santamore, MD, PhD
Javier P. Sanchez, MD, Giuseppe Carminati, MD, Luigi Di Biase, MD
Ferruccio Franzosi, MD, Luigi Di Biase, MD, PhD

Left atrial appendage morphology assessment for risk stratification of embolic stroke in patients with atrial fibrillation: A meta-analysis

Hernanillo Lopez, MB, Juan Caro Roldan, MB, David E. Brito, MD, Jorge Romanos, MB, MD
Pedro A. Villalobos, MB, Cecilia Benavente, MB, Robert Fialho, MB, MD
Andres Anostrano, MB, David D. Fisher, MD, FRH
Tonye Etomi, MB, MD
Maria Garcia, MB, Andreia Portela, MD, PhD
Luigi Di Biase, MD, PhD, FRH

Keywords: "Metaphase Medical Center, Albert Einstein College of Medicine, Bronx, New York, "Atria-Adaptive Center, Albert Einstein College of Medicine, Bronx, New York, "Jewish Hospital, Washington University, St Louis, Missouri, "Mayo Clinic, Rochester, Minnesota, "Mount Sinai Medical Center, New York, New York, "Northwestern University, Chicago, Illinois, "University of Chicago, Chicago, Illinois, "University of California, San Diego, California""
Who is high risk?

- Ischemic stroke despite adequate anticoagulation
- High thromboembolic risk but previous intra-cerebral bleed on anticoagulants
- High thrombo-embolic risk but previous life-threatening bleed on anticoagulants at correct INR
- High thrombo-embolic risk but previous major bleed on anticoagulants
- High thromboembolic risk with major risk of bleeding (HASBLED ≥ 3)
- High thromboembolic risk and time in therapeutic range < 65%
- High thromboembolic risk and unwilling to take anticoagulants
- Treatment of choice – best therapeutic option – patient choice

Watchman Device

Frame: Nitinol structure
- Available sizes: 21, 24, 27, 30, 33 mm (diameter)
- 10 fixation barbs around device perimeter engage LAA tissue
- Contour shape accommodates most LAA anatomy

Fabric Cap: Polyethyl terephthalate (PET)
- Prevents harmful emboli from exiting during the healing process
- 160 micron filter
Watchman Device, Indications

The WATCHMAN Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

- Are at increased risk for stroke and systemic embolism based on CHADS\textsubscript{2} or CHA\textsubscript{2}DS\textsubscript{2}-VASc scores and recommended for anticoagulation therapy.
- Are deemed by their physicians to be suitable for warfarin; and
- Have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

Pre-procedural LAA Anatomy Assessment

- Assess the following LAA features:
  - Ostium size and shape
  - Number of lobes, location
  - Working length in the LAA
  - Pectinate features
- Assess less challenging vs. more challenging anatomies
  - Relationship of LAA to LUPV/MV
  - Categorize by LAA Type
  - Windsock, Chicken wing or Broccoli

Use of Fluoro & TEE for Transseptal puncture

4 Steps Prior to Release (PASS):

- Position – device is distal to or at the ostium of the LAA
- Anchor - fixation barbs engaged / device is stable
- Size – device is compressed 8-20% of original size
- Seal - device spans ostium, all lobes of LAA are covered
  (if necessary, device can be recaptured (partial or full))
Device Endothelization

Canine Model - 30 Day
Canine Model - 45 Day
Human Pathology - 5 Months Post-implant (Non-device related death)

Protect AF

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PROTECT AF</th>
<th>CAP Registry</th>
<th>PREVAIL Registry</th>
<th>CAP2 Registry</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHADS2 Score</td>
<td>2.2 ± 1.2</td>
<td>2.5 ± 1.2</td>
<td>2.6 ± 1.0</td>
<td>2.7 ± 1.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CHADS2 Risk Factors (% of Patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>26.9</td>
<td>23.3</td>
<td>23.1</td>
<td>27.1</td>
<td>0.084</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.8</td>
<td>94.6</td>
<td>88.8</td>
<td>94.5</td>
<td>0.15</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>45.1</td>
<td>53.6</td>
<td>51.6</td>
<td>59.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>35.2</td>
<td>37.4</td>
<td>74.9</td>
<td>33.7</td>
<td>0.025</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>18.5</td>
<td>27.8</td>
<td>30.4</td>
<td>29.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CHA2 DS_VASc</td>
<td>3.5 ± 1.6</td>
<td>3.9 ± 1.5</td>
<td>4.0 ± 1.8</td>
<td>4.5 ± 1.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Implantation Success Rate

PREVAIL Implant Success
No difference between new and experienced operators
Experienced Operators
• n = 26
• 96%
New Operators
• n = 24
• 93%

Implant success defined as deployment and release of the device into the left atrial appendage

Procedural Safety Profile

7-Day Safety Events

CAP PREVAIL CAP2
n=232 n=231

PROTECT AF
1st Half 2nd Half
Learning Curve

CAP PREVAIL CAP2
n=579 n=269 n=566


WATCHMAN Performance
Consistent Across All 4 Data Sets
### Warfarin Arms of PROTECT-AF & PREVAIL

**Ischemic Stroke Rates: Observed vs Expected**

<table>
<thead>
<tr>
<th>Trial (Warfarin Arm)</th>
<th>Ischemic Stroke Rate per 100 pt-yrs</th>
<th>Mean CHADS2</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREVAIL</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>PROTECT AF</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>RE-LY</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>ROCKET AF</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>ENGAGE</td>
<td>2.8</td>
<td></td>
</tr>
</tbody>
</table>

**Trial (Warfarin Arm) Output**

<table>
<thead>
<tr>
<th>Event</th>
<th>Hazard Ratio (95% CI)</th>
<th>Posterior Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy</td>
<td>0.61 (0.42, 0.97)</td>
<td>&gt;99.9%</td>
</tr>
<tr>
<td>Stroke (all)</td>
<td>0.68 (0.42, 1.07)</td>
<td>99.9%</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Death (CV/unexplained)</td>
<td>0.44 (0.26, 0.73)</td>
<td>&gt;99.9%</td>
</tr>
</tbody>
</table>

**HR**

- Favors warfarin
- Favors WATCHMAN

**D.Holmes et al, TCT Presentation, September 2014.**

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### PROTECT-AF & PREVAIL

**in Relative Context Combined Analysis**

<table>
<thead>
<tr>
<th>Event</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>0.79</td>
<td>0.22</td>
</tr>
<tr>
<td>All stroke or SE</td>
<td>1.02</td>
<td>0.34</td>
</tr>
<tr>
<td>Ischemic stroke or SE</td>
<td>1.05</td>
<td>0.33</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0.22</td>
<td>0.004</td>
</tr>
<tr>
<td>Circumvented death</td>
<td>0.68</td>
<td>0.008</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.73</td>
<td>0.07</td>
</tr>
<tr>
<td>Major bleed, all</td>
<td>1.08</td>
<td>0.56</td>
</tr>
<tr>
<td>Major bleeding, non procedure-related</td>
<td>0.51</td>
<td>0.002</td>
</tr>
</tbody>
</table>

**Hazard Ratio (95% CI)**

- Favors WATCHMAN
- Favors warfarin

---

### Protect AF, 4y results

<table>
<thead>
<tr>
<th>Event Rate</th>
<th>(per 100 Pt-yrs)</th>
<th>Rate Ratio (95% CrI)</th>
<th>Posterior Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy</td>
<td>2.2</td>
<td>3.7</td>
<td>0.61 (0.42, 0.97)</td>
</tr>
<tr>
<td>Stroke (all)</td>
<td>1.5</td>
<td>2.2</td>
<td>0.68 (0.42, 1.07)</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>0.2</td>
<td>0.1</td>
<td>N/A</td>
</tr>
<tr>
<td>Death (CV/unexplained)</td>
<td>1.0</td>
<td>0.3</td>
<td>0.44 (0.26, 0.73)</td>
</tr>
</tbody>
</table>

**Primary efficacy**

- 95.4%

**Stroke (all)**

- 83%

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### PROTECT AF: 5-Year Primary Efficacy Events
PROTECT AF/PREVAIL Pooled Analysis: Less Bleeding with WATCHMAN 6 Months Post-Implant

Free of Major Bleeding Event (%)

<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>Warfarin + Aspirin</th>
<th>Aspirin</th>
<th>Aspirin + Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>WATCHMAN</td>
<td>66</td>
<td>84</td>
<td>71%</td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>180</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin +</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Relative Reduction in Major Bleeding after cessation of antithrombotics

HR = 0.29
p<0.001

Preventing Stroke in Non-Valvular AF
Effectiveness of Different Strategies

Use of non-warfarin oral anticoagulants instead of warfarin during left atrial appendage closure with the Watchman device

- Retrospective multicenter (5 centers) study of consecutive patients undergoing Watchman implantation.
- Transesophageal echocardiography or chest computed tomography was performed between 6 weeks and 4 months post-implant to assess for device-related thrombosis.
- Bleeding and thromboembolic events also were evaluated at the time of follow-up.
- 214 patients received NOACs (46% apixaban, 46% rivaroxaban, 7% dabigatran, and 1% edoxaban).
- Either uninterrupted (82%) or a single-held-dose (16%) fashion.
- 212 patients, control group, with uninterrupted warfarin.
Use of non-warfarin oral anticoagulants instead of warfarin during left atrial appendage closure with the Watchman device

<table>
<thead>
<tr>
<th>Separate Events</th>
<th>Watchman (n=212)</th>
<th>Warfarin (n=214)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major complications</td>
<td>6 (2.8%)</td>
<td>8 (3.7%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>4 (1.9%)</td>
<td>4 (1.9%)</td>
<td>1</td>
</tr>
<tr>
<td>LAA thrombosis</td>
<td>13 (6.1%)</td>
<td>13 (6.1%)</td>
<td>1</td>
</tr>
<tr>
<td>LAA embolism</td>
<td>2 (0.9%)</td>
<td>3 (1.4%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Other complications</td>
<td>26 (12.2%)</td>
<td>29 (13.6%)</td>
<td>1</td>
</tr>
</tbody>
</table>

Results:
- **Objective:** Non-warfarin anticoagulants with comparison to warfarin
- **Background:** Atrial fibrillation (AF) is associated with an increased risk of thromboembolic events, mainly stroke, and is the main indication for anticoagulation. Warfarin, an oral anticoagulant, is the standard therapy for stroke prevention in AF patients, but it requires frequent monitoring of the international normalized ratio (INR) to achieve the therapeutic range (2-3).
- **Methods:** Multicenter, retrospective, randomized clinical trial comparing non-warfarin oral anticoagulants (NOACs) to warfarin in AF patients who were candidates for left atrial appendage closure (LAAC) with the Watchman device.
- **Patient population:** Inclusion criteria were AF patients with left atrial thrombi, previous cerebrovascular accident (CVA), and CHADS2 score ≥2.
- **Interventions:** Patients were randomly assigned to receive either NOACs (apixaban, rivaroxaban, edoxaban) or warfarin for a 6-month follow-up period after LAAC.
- **Outcomes:** The primary endpoint was the occurrence of thromboembolism, major bleeding, and major adverse cardiovascular (MACE) events.

**Conclusion:**
- NOACs were non-inferior to warfarin in reducing the risk of thromboembolic events, major bleeding, and MACE events after LAAC.
- NOACs demonstrated a lower risk of major bleeding compared to warfarin, making them a safer option for anticoagulation post-LAAC.

**Case 1:**
- 63 y.o. unfortunate female with long-standing persistent AF and: - ASD P/S surgery 1993 - Mitral valve repair - AF ablation 2005 - Hypertension - Obstructive sleep
- Admitted 73 y.o. female with persistent atrial fibrillation not on anticoagulation due to fall risk, CAD, HTN, CKD.

**Case 2:**
- 73 y.o. female with persistent atrial fibrillation not on anticoagulation due to fall risk, CAD, HTN, CKD.
- Admitted with and tempo-parietal stroke and have hemorrhagic transformation when started on anticoagulation.
- The patient was evaluated with Neurology and she was deemed to be a possible candidate for a short-term anticoagulation and presented for transesophageal echocardiogram.
Lariat Suture Possible Candidates

- Absolute contra-indications to systemic OAC (active GI bleeding, ICH...)
- Candidate patient for Watchman but challenging LAA/unsuitable anatomy.
- aMAZE trial.

Use of LARIAT Suture Delivery Device for Left Atrial Appendage Closure: FDA Safety Communication

- **Date Issued:** July 13, 2015
- The FDA conducted a search of the Manufacturer and User Facility Device Experience (MAUDE) database for reports of adverse events with the use of the LARIAT Suture Delivery Device and its associated devices.
- We identified 45 adverse events through June 30, 2015, that occurred in patients undergoing LAA closure procedures with the LARIAT Suture Delivery Device and/or its associated devices.
- These reports describe 6 patient deaths and other serious medical complications including laceration and/or perforation of the heart, complete LAA detachment from the heart, bleeding (hemorrhage), low blood pressure (hypotension), fluid collection around the heart (pericardial effusion), fluid collection around the heart that causes low blood pressure and decreased heart function leading to shock (cardiac tamponade), and fluid collection around the lung (pleural effusion).
- Of the 45 adverse events reported to the FDA, 34 (approximately 75%) resulted in the need to perform emergency heart surgery.

Use of LARIAT Suture Delivery Device for Left Atrial Appendage Closure: FDA Safety Communication

- Be aware that the safety and effectiveness of the LARIAT Suture Delivery Device to close the LAA and prevent stroke in patients with atrial fibrillation has not been established.
- To reduce the risk of stroke in patients with atrial fibrillation, consider treatment options for which safety and effectiveness have been established.
- Prior to treatment, inform your atrial fibrillation patients of the benefits and risks of the available treatment options to help prevent stroke.
- Report any adverse events associated with the use of the LARIAT Suture Delivery Device and/or its associated devices to the FDA and the manufacturer.
Background—A dry epicardial access (EA) is increasingly used for advanced cardiovascular procedures. Conventionally, used large bore needles (Tuohy or Pajunk needle; LBN) have been associated with low but definite incidence of major complications with EA. Use of micropuncture needle (MPN) may decrease the risk of complications. We intended to compare the outcomes of two different techniques.

Methods and Results—We report a multicenter observational study of consecutive patients who underwent EA for ventricular tachycardia ablation or Lariat procedure using the LBN or MPN. Oral anticoagulation was stopped before the procedure. Baseline characteristics and procedure-related complications were collected and compared. Of the 404 patients, 202 patients used in LBN and 202 patients were used in MPN. There was no significant difference in the incidence of inadvertent myocardial puncture (7.6% versus 6.8%, Pro.09), other complications associated with MPN (1.6% versus 4.9%, Pro.06). However, there was a significantly higher rate of large pericardial effusions with LBN compared to MPN (8.1% versus 2.3%, Pro.04). The incidence of pleural effusions were not significantly different between both (1.6% versus 2.3%, Pro.64). LBN group had an increase in other complications compared with MPN (open heart surgery to repair cardiac laceration [8 versus 0], injury to liver [5 versus 0], coronary [1 versus 0], and superior epigastric artery requiring surgical exploration [3 versus 0]).

Conclusions—The use of MPN is associated with decreased incidence of major complications, and the need for surgical repair and routine use should be considered for EA.

We report a multicenter observational study of consecutive patients who underwent EA for ventricular tachycardia ablation or Lariat procedure using the LBN or MPN.

Oral anticoagulation was stopped before the procedure.

404 patients, LBN was used in 40% and MPN in 54% of patients.

There was no significant difference in the incidence of inadvertent puncture of myocardium between LBN and MPN (7.6% versus 6.8%, Pro.09).

Significantly higher rate of large pericardial effusions with LBN compared with MPN (8.1% versus 2.3%, Pro.04).

The incidence of pleural effusions were not significantly different between both (1.6% versus 2.3%, Pro.64).

LBN group had an increase in other complications compared with MPN (open heart surgery to repair cardiac laceration [8 versus 0], injury to liver [5 versus 0], coronary [1 versus 0], and superior epigastric artery requiring surgical exploration [3 versus 0]).
Impact of Peri-procedural Colchicine on Post-procedural management in Patients undergoing on Left Atrial Appendage Ligation using LARIAT

Sampath Gunda MD*¥, Yeruva Madhu Reddy MD FACC FHRS*¥, Jayant Nath MD*, Ryan Ferrell MD*, Steven Bormann MD*, Hosakote Nagaraj MDα, Moustapha Atoui MD*, Abdi Rasekh MDβ, Christopher R. Ellis MD∞, Nitish Badhwar MDµ, Randall J. Lee, MD PhDµ, Luigi Di Biase MD PhDπ, Moussa Mansour MD FACC FHRS Ω, Jeremy N. Ruskin MD, Andrea Natale MD FHRS∑, Matthew Earnest MD* and Dhanunjaya R. Lakkireddy MD FACC FHRS*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Colchicine group</th>
<th>Standard group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericarditis (%)</td>
<td>10 (4)</td>
<td>16 (16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Delayed pericardial Effusion (%)</td>
<td>4 (1.6)</td>
<td>3 (3)</td>
<td>0.42</td>
</tr>
<tr>
<td>Pleural Effusion (%)</td>
<td>4 (1.6)</td>
<td>9 (9)</td>
<td>0.003</td>
</tr>
<tr>
<td>GI Side effects (%)</td>
<td>25 (10)</td>
<td>1 (1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pericardial drain volume (ml)</td>
<td>186± 84</td>
<td>351± 83</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of days with chest pain</td>
<td>3.6± 1</td>
<td>6.6± 1.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>2.3± 0.8</td>
<td>3.8± 1.8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

EXPERIENCE OF PERCUTANEOUS LEFT ATRIAL APPENDAGE SUTURE LIGATION: RESULTS FROM A UNITED STATES MULTICENTER EVALUATION

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<table>
<thead>
<tr>
<th>Procedure variable</th>
<th>Total</th>
<th>LB needle (n=286)</th>
<th>MP needle (n=409)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure related mortality</td>
<td>1 (0.14)</td>
<td>0 (0)</td>
<td>1 (0.24)</td>
<td>NA</td>
</tr>
<tr>
<td>Patients needing open heart surgery</td>
<td>10 (1.44)</td>
<td>9 (3.15)</td>
<td>1 (0.24)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cardiac perforations without need for cardiac surgery</td>
<td>4 (0.60)</td>
<td>1 (0.37)</td>
<td>3 (0.73)</td>
<td>0.48</td>
</tr>
<tr>
<td>Patients needing transfusion</td>
<td>9 (1.30)</td>
<td>7 (4.25)</td>
<td>2 (0.45)</td>
<td>0.02</td>
</tr>
<tr>
<td>Stroke in the peri-procedural period</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Injury to the supero-inferior coronary artery</td>
<td>4 (0.60)</td>
<td>2 (0.59)</td>
<td>2 (0.58)</td>
<td>0.7</td>
</tr>
<tr>
<td>Total</td>
<td>38 (5.47)</td>
<td>29 (10.14)</td>
<td>9 (2.20)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
Prospective observational study of patients with persistent AF referred for AF ablation.

Patients underwent LAA ligation with LARIAT procedure before undergoing AF ablation (LARIAT group).

Age and sex-matched persistent AF patients undergoing AF ablation during the same time frame were included in the control group (ablation-only group).

Results:

- A total of 138 patients were included in the study, with 69 patients in the LARIAT group.
- Left atrial (LA) size, CHADS2, CHADSVasc, and HAS-BLED scores were higher in the LARIAT group.
- No differences in the type of lesions during AF ablation between the groups.
- The primary outcome (freedom from AF) at 12 months did not differ significantly between the LARIAT and ablation-only groups.
- Conclusions:

  - In patients with persistent AF, addition of LAA ligation with the LARIAT device to conventional ablation appears to improve the success rate of AF ablation.

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**MAZE Protocol Synopsis**

**Principal Purpose:** Evaluate the additional efficacy of LARIAT to decrease the 12-month rate of AF, and to confirm an acceptable safety profile.

**Patient Population:** Patients (18-80 y.o.) with documented persistent or longstanding persistent AF (< 3 yrs continuous AF) planned for catheter ablation.

**Design:** Prospective, multicenter, RCT (2:1) Bayesian Adaptive Design with multiple interim analyses; 400 – 600 subjects; ~50 sites.

2 randomized stages: Stage 1 ≤ 175 subjects; interim safety and performance analysis of first 100.

**Investigational Tx:** LARIAT LAA ligation followed by PVI catheter ablation (4 weeks).

**Control Tx:** PVI catheter ablation without LAA ligation.

**Rationale and design**


**Primary Endpoints**

**Primary Effectiveness Endpoint:** Freedom from episodes of AF > 30 seconds and no requirement for new Class I or III AAD therapy at 12 months post PVI, measured by 24-hr Holter or symptomatic event monitoring.

**Primary Safety Endpoint:** The incidence of significant LARIAT device or procedure-related SAEs occurring within 30 days after the LAA ligation procedure (Performance Goal).
• 15 y.o boy with incessant focal atrial tachycardia
• Origin from the LAA on mapping
• Recurrence after an ablation procedure from distal coronary sinus (earliest site).

Electrical Isolation with Atriclip:

Thoracoscopic Appendage Exclusion With an Atriclip Device As a Sole Treatment for Focal Atrial Tachycardia


Surface and epicardial ECG during the stimulation of the LAA demonstrating an exit block from the LAA.

Surface and epicardial ECG during the stimulation of the LA demonstrating an entry block to the LAA.
**Atriclip**

- Most of the observational data in pts with concomitant OHS
- Theoretically no post procedural OAC needed
- Electrical isolation
- Great option in complex anatomy – Pts who are not candidates for percutaneous closure
- Requires surgery

**LAA Exclusion systems**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Watchman</th>
<th>Lariat</th>
<th>Atriclip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maker</td>
<td>Atritech (Boston scientific)</td>
<td>Atritech</td>
<td>Senterheart</td>
</tr>
<tr>
<td>Approval</td>
<td>CE and FDA</td>
<td>CE and FDA</td>
<td>CE and FDA</td>
</tr>
<tr>
<td>Approach</td>
<td>Endocardial</td>
<td>Endo &amp; Epicardial</td>
<td>Epicardial</td>
</tr>
<tr>
<td>Type</td>
<td>Deployable</td>
<td>Deployable</td>
<td>Deployable</td>
</tr>
<tr>
<td>Hardware left in heart</td>
<td>Yes</td>
<td>No</td>
<td>Yes (Epicardial)</td>
</tr>
<tr>
<td>Can be used after open heart surgery</td>
<td>Yes</td>
<td>No</td>
<td>Yes (Possible)</td>
</tr>
<tr>
<td>Retrievable</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Protect AF, Long term 5y results

Study Design & Objective
Prospective, randomized 2:1, non-inferiority trial of LAA closure vs. warfarin in non-valvular AF patients for prevention of stroke

Primary Endpoint
Composite end point of stroke, cardiovascular death or systemic embolization

Secondary Goals
Mitra valve disease, device embolization or pericardial effusion

Statistical Plan
All analyses by intention to treat.
Bayesian (stratified for CHADS2 score): Primary Efficacy and Safety endpoints
Cox Proportional: All Secondary Analyses

Patient Population
N=302
Mean CHADS2=2.3, CHA2DS2-VASc=3.5

Key Inclusion Criteria
Paroxysmal/Persistent/Permanent AF
CHA2DS2 ≥ 1 (93% had a CHA2DS2-VASc Score ≥ 2)
Eligible for long term warfarin therapy

Mean Follow-Up
2,717 patient-years, 48 months

Number of Sites
35 in the United States and Europe
Enrollment Feb 2005 – June 2008

The WATCHMAN™ LAAC Device is the most studied LAAC device and the only one proven with long term data from randomized trials or multi-center registries
Five studies, 1,940 patients, nearly 60 patient-years of follow-up

The WATCHMAN Device can be implanted safely1, enables patients to discontinue warfarin2 and reduces AF stroke risk comparably to warfarin:
- 95% implant success rate3
- 92% warfarin cessation after 45 days, 96% after 1 year

WATCHMAN™ therapy demonstrated comparable stroke risk reduction, and statistically superior reductions in hemorrhagic stroke, disabling stroke and cardiovascular death compared to warfarin over long term follow-up4:
- 32% in all-cause stroke
- 85% in hemorrhagic stroke
- 63% in disabling stroke
- 56% in cardiovascular death

The WATCHMAN™ LAAC Device is the most studied LAAC device and the only one proven with long term data from randomized trials or multi-center registries. Five studies, 1,940 patients, nearly 60 patient-years of follow-up. The WATCHMAN Device can be implanted safely, enables patients to discontinue warfarin and reduces AF stroke risk comparably to warfarin: 95% implant success rate. WATCHMAN therapy demonstrated comparable stroke risk reduction, and statistically superior reductions in hemorrhagic stroke, disabling stroke and cardiovascular death compared to warfarin over long term follow-up: 32% in all-cause stroke, 85% in hemorrhagic stroke, 63% in disabling stroke, 56% in cardiovascular death.