The Left Atrium, Clot and Atrial Fibrillation: Device Therapy to Prevent Stroke

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Disclosures

I have no conflict of interests to disclose

Some slides courtesy of
Raul Weiss MD, Professor of Medicine
Director Electrophysiology Fellowship Program
The Ohio State University Wexner Medical Center
Atrial Fibrillation – Quick Facts

- Most common type of arrhythmia

- The estimated cost of the treatment of atrial fibrillation in 2005 was $6.65 billion per year

- An estimated 2.66 million people will have atrial fibrillation in 2010

- As many as 12 million people will have the condition by 2050

- Incidence increases with age
  Median age is 66.8 (M), 74.6 (F)

- African Americans experience atrial fibrillation at much lower rates than whites

- Risk factors for atrial fibrillation:
  - High blood pressure, heart failure, diabetes, advanced age, hyperthyroidism, and heart disease

- Stroke and heart failure are the two most common complications of atrial fibrillation

- Atrial fibrillation is responsible for 15 to 20 percent of ischemic strokes (5 times)

Source:
http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/docs/fs_atrial_fibrillation.pdf
Approximately 90% of left atrial clots come from the left atrial appendage (LAA)

Johnson and colleagues in a report of prophylactic LAA excision in 437 patients from 1995 to 1997 “Our Most Lethal Human Attachment”
Left Atrial Appendage (LAA) Anatomy

LAA - lateral wall of the heart
Close to the LCx
Great cardiac vein
< 1 cm of the MV annulus
Orifice of the LSPV
Diagram of a Left Atrial Appendage Shows lobes

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

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: Orifice Size as a Function of Age for Males and Female

Left atrial appendage (LAA) Publications

- LAA obliteration - 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

# Stroke Risk secondary to Atrial Fibrillation: CHADS(2) Score

<table>
<thead>
<tr>
<th>CHADS(2) Score</th>
<th>CHADS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>+1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>+1</td>
</tr>
<tr>
<td>Age 75+</td>
<td>+1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>+1</td>
</tr>
<tr>
<td>Stroke or History of Cerebral Ischemia</td>
<td>+2</td>
</tr>
</tbody>
</table>

**CHADS:** 0 = ASA or nothing, 1 = ASA or warfarin, ≥ 2 = warfarin

Newer anticoagulants in Atrial Fibrillation
Surgical Techniques for LAA Occlusion

- Exclusion
  - Sutures
    - Epicardial
    - Endocardial
  - Exclusion Device
    - AtriClip
    - TigerPaw® System II

- Excision
  - Stapled excision
  - Surgical clamp and excision
Surgical Techniques for LAA Exclusion

Epicardial suture exclusion

Endocardial suture exclusion

Surgical Techniques for LAA Occlusion
Surgical Techniques for LAA Occlusion
Surgical Techniques for LAA Excision

Surgical Techniques for LAA Excision
# Outcomes: Surgical

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Country</th>
<th>No. Studied</th>
<th>Method of Closure</th>
<th>Closure Success Rate, $^a$ %</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></td>
<td></td>
<td></td>
<td>Excision</td>
<td>100</td>
<td>Positive</td>
</tr>
<tr>
<td>Schneider, 2005 [41]</td>
<td>Germany</td>
<td>6</td>
<td>Endocardial suture</td>
<td>17</td>
<td>Negative</td>
</tr>
<tr>
<td>Healey, 2005 [28]</td>
<td>Canada</td>
<td>77</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></td>
</tr>
<tr>
<td>Kanderian, 2008 [29]</td>
<td>USA</td>
<td>137</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></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stapler</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bakhtiary, 2008 [33]</td>
<td>Germany</td>
<td>259</td>
<td>Clamp and epicardial suture</td>
<td>100$^b$</td>
<td>Positive</td>
</tr>
</tbody>
</table>

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Comparison of Surgical Left Atrial Appendage Closure Techniques

Exclusion of the left atrial appendage with a novel device: Early results of a multicenter trial

Gorav Ailawadi, MD, a Marc W. Gerdisch, MD, b Richard L. Harvey, MD, c Ralph J. Damiano, Jr, MD, d Thomas Salamon, MD, e and Michael J. Mack f

Objective: Up to 90% of embolic strokes that occur in patients with atrial fibrillation are associated with left atrial appendage. Exclusion of the left atrial appendage during cardiac surgery, especially in patients with atrial fibrillation or at high risk for development of stroke, is becoming an accepted practice. We report the initial results of a multicenter Food and Drug Administration trial to assess the efficacy and safety of a left atrial appendage exclusion clip.

Methods: Patients undergoing elective cardiac surgery via median sternotomy with acute or chronic heart failure, hypertension, age > 75 years, diabetes mellitus, and left atrial diameter ≥ 40 mm were eligible for concomitant AtriClip (Atricure Inc., Westchester, Ohio) device (sizes 40, 45, and 50 mm) implantation. The efficacy of left atrial appendage exclusion was assessed at 30 days, and efficacy of left atrial appendage exclusion was assessed by transesophageal echocardiography, and follow-up by computed tomography (CT) and 3-month follow-up (by computed tomography angiography or transesophageal echocardiography).

Results: A total of 71 patients (mean age, 73 years) undergoing open cardiotomy was enrolled in the study. The left atrial appendage in 1 patient was too small for the AtriClip device, and the remaining 70 patients had successful placement of an AtriClip device. Left atrial appendage exclusion was confirmed in 67 of 70 patients (95.7%). Although there were no adverse events related to the device, 1 patient died and 65 of 70 patients (92.9%) were available for 3-month follow-up. Of the 65 patients who underwent imaging, 60 of 61 patients (98.4%) had successful left atrial appendage exclusion by CT and 58 of 59 patients (98.3%) had successful left atrial appendage exclusion by transesophageal echocardiography imaging.

Conclusions: In this small study, safe and atraumatic exclusion of the left atrial appendage can be performed during open cardiac surgery with the AtriClip device with greater than 95% success and appears to be durable in the short term by imaging. Long-term studies are needed to evaluate the efficacy in the prevention of stroke. (J Thorac Cardiovasc Surg 2011;142:1002-9)
Transcatheter Techniques for LAA Occlusion

- Surgical Techniques
  - Exclusion
    - Sutures
      - Epicardial
      - Endocardial
    - Exclusion Device
      - AtriClip®
      - TigerPaw® System II
  - Excision
    - Stapled excision
    - Surgical clamp and excision

- Transcatheter
  - Occlusion
    - WATCHMAN®
    - Amplatzer Cardiac Plug
  - Exclusion
    - LARIAT
The WATCHMAN® Device

Properties

- Umbrella-like, self-expanding nitinol frame
- Anchors
- Permeable fabric cover

Deployment

- Transseptal catheter-based approach

Purpose

- Seal off the left atrial appendage to help prevent the estimated 80%-90% of strokes.
The AMPLATZER™ Cardiac Plug

Properties

• Self-expanding nitinol mesh
• 2 polyester patches
• Two parts: A lobe and a disc with a central waist

Deployment

• Transseptal catheter-based approach

Purpose

• Seal off the left atrial appendage
The AMPLATZER™ Cardiac Plug
The AMPLATZER™ Cardiac Plug

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:**
  - 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
  - Afterwards long-term aspirin is recommended
Properties

• (A) Endocardial magnet-tipped and epicardial magnet-tipped guidewire

• (B) a 15-mm compliant occlusion balloon catheter to identify the LAA os with TEE

• (C) the LARIAT suture delivery device with pre-tied size 0 Teflon-coated, braided polyester suture (blue) mounted within a radiopaque adjustable snare.

• (D) Components as a system

Deployment

• Transseptal catheter-based approach in combination with intrapericardial approach

Purpose

• Mimic “surgical exclusion”
Inclusion Criteria:

- Age 18 years or older
- Non-valvular AF
- CHADS 1 or higher
- Poor candidate or ineligible for warfarin therapy and/or a warfarin failure (i.e., transient ischemic attack or stroke while on warfarin therapy)
- Life expectancy of at least 1 year

Exclusion Criteria:

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

Exclusion Criteria Based on LAA Anatomy:

- a LAA width 40 mm;
- Superiorly oriented LAA with the LAA apex directed behind the pulmonary trunk
- Bilobed LAA or multilobed LAA in which lobes were oriented in different planes exceeding 40 mm
- Posteriorly rotated heart

The LARIAT Device: Additional Considerations

Fluoroscopic Guidance: LARIAT Closure of LAA

Outcomes: The LARIAT Device

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%)

PT 9: Pericardial effusion due to inadvertent RV dilation
PT 24: Pericardial effusion at initiation due to epigastric vessel laceration
PT 25: Anatomic contraindication prior to transseptal (dilated RA)
PT 93: Unable to capture LAA due to localized adhesions on LAA sulcus

Outcomes: The LARIAT Device

<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>1 (1.1%)</td>
</tr>
</tbody>
</table>

**End-of-procedure closure (n = 85)**
- Complete or <1-mm leak: 82 (96%)
- <2-mm leak: 2 (3%)
- <3-mm leak: 1 (1%)

**1 day post-procedure closure by TEE (n = 85)**
- Complete or <1-mm leak: 81 (95%)
- <2-mm leak: 3 (4%)
- <3-mm leak: 1 (1%)

**30 days post-procedure closure by TEE (n = 85)**
- Complete or <1-mm leak: 81 (95%)
- <2-mm leak: 3 (4%)
- <3-mm leak: 1 (1%)

**90 days post-procedure closure by TEE (n = 81)**
- Complete or <1-mm leak: 77 (95%)
- <2-mm leak: 3 (4%)
- <3-mm leak: 1 (1%)

**1 year post-procedure closure by TEE (n = 65)**
- Complete or <1-mm leak: 64 (98%)
- <2-mm leak: 1 (2%)

**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

Outcomes: WATCHMAN

- PROTECT AF
- Continuous Access
- ASAP
- PREVAIL
Outcomes: WATCHMAN – PROTECT AF

- 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

Baseline Risk Factors

<table>
<thead>
<tr>
<th>CHADS2</th>
<th>WATCHMAN Device (%)</th>
<th>Warfarin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33.9%</td>
<td>27%</td>
</tr>
<tr>
<td>2</td>
<td>34.1%</td>
<td>36.1%</td>
</tr>
<tr>
<td>3</td>
<td>19%</td>
<td>20.9%</td>
</tr>
<tr>
<td>4</td>
<td>8%</td>
<td>9.8%</td>
</tr>
<tr>
<td>5</td>
<td>4.1%</td>
<td>4.1%</td>
</tr>
<tr>
<td>6</td>
<td>0.9%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Average age for WATCHMAN® was 71.7 years 8.8 years

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.

Outcomes: WATCHMAN – PROTECT AF

- 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
Outcomes: WATCHMAN – PROTECT AF

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.

Outcomes: WATCHMAN – PROTECT AF……
Rolling into continued access registry (CAP)

- 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 CHADS₂</td>
<td>2.2</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Warfarin Discontinuation

95% of patients overall discontinued warfarin at 45 days

Implantation success defined as device implantation followed by discontinuation of warfarin

Outcomes: WATCHMAN – PROTECT AF, CAP

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)
Rates of pericardial effusion 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

32% reduction in rates of pericardial effusion as experience increased

Outcomes: WATCHMAN – PROTECT AF, CAP and procedure related safety events

- 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


### Annual risk of stroke with secondary prevention of aspirin or warfarin

- **Prior TIA**
  - Aspirin: 3%
  - Warfarin: 4%
- **Prior Stroke**
  - Aspirin: 7%
  - Warfarin: 11%
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

Outcomes: WATCHMAN – ASAP Registry
Aspirin and Plavix® Registry

Rate of Success with implantation in warfarin contraindicated patients

94.7% successfully implanted

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
Outcomes: WATCHMAN – ASAP Registry
Aspirin and Plavix® Registry

Ischemic Stroke Rate (%/pt-yr)

7.3%

1.7%

77% Reduction

Expected, based on CHADS₂ Score
Observed rate in ASAP

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
Outcomes: WATCHMAN – ASAP Registry
Aspirin and Plavix® Registry

Ischemic Stroke

- Expected, based on CHADS₂ Score
- Expected, if Clopidogrel was used throughout follow-up
- Observed rate in ASAP

Reddy, ASAP WATCHMAN, HRS 2012, Boston, MA
<table>
<thead>
<tr>
<th>Study Objective:</th>
<th>To evaluate the long term embolic stroke rate of patients implanted with the WATCHMAN® left atrial appendage closure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Design:</td>
<td>Prospective, multicenter</td>
</tr>
<tr>
<td>Primary Endpoint:</td>
<td>Embolic stroke</td>
</tr>
<tr>
<td>Patient Population:</td>
<td>n=66; Mean age=68.5±8 years; Mean CHADS₂ score=1.8±1.1</td>
</tr>
<tr>
<td>Mean Follow Up:</td>
<td>73±25 months</td>
</tr>
<tr>
<td>Number of Sites:</td>
<td>8 (US and Germany)</td>
</tr>
<tr>
<td>Presented by:</td>
<td>Peter B. Sick, MD,; ESC 2012</td>
</tr>
</tbody>
</table>

Sick, et al., WATCHMAN Pilot data; ESC 2012, Munich, Germany
Ischemic Stroke

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

*Sick, et al., WATCHMAN Pilot study; ESC 2012, Munich, Germany

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

Expected, based on CHADS₂ Score

Observed rate in 6 year follow up

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

Mobius–Winkler, et al., WATCHMAN Pilot data; ESC 2012, Munich, Germany
All stroke

- 93% had CHA$_2$DS$_2$VASc score > 2
- Average CHA$_2$DS$_2$Vasc score: 3.5
- Expected risk of stroke: 3%
- Observed stroke rate: 2%
- 37.5% reduction compared to expected

Mobius–Winkler, et al., WATCHMAN Pilot data; ESC 2012, Munich, Germany
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
Three trials of the WATCHMAN® Device have reached their primary endpoints; a fourth is finished enrolling.

<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></td>
<td>Warfarin contraindicated patients</td>
<td>Patients able to take warfarin</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>finished</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 (P=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></td>
<td>HR 1.69 (1.01–3.19)</td>
<td>Reduction in pericardial effusions vs PROTECT AF (P=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
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.
Conclusion: Better Refinement

Surgical Excision (Appendagectomy)
- Can create pouch with stagnant blood flow
- High invasiveness

Transcatheter Device Closure
- Minimally invasive nature
- Intended as an alternative to warfarin therapy for patients with non-valvular atrial fibrillation

The Lariat device
- Commercially available
- No good prospective data
- Approved as a “surgical suture”