MHIF FEATURED STUDY: OPTION
Comparison of Anticoagulation with Left Atrial Appendage Closure after AF Ablation

DESCRIPTION: The primary objective of this study is to determine if left atrial appendage closure with the WATCHMAN FLX Device is a reasonable alternative to oral anticoagulation following percutaneous catheter ablation for high risk patients with non-valvular atrial fibrillation.

STUDY DESIGN: This study is a prospective, randomized, multi-center, global investigation to determine if left atrial appendage closure with the WATCHMAN FLX Device is a reasonable alternative to oral anticoagulation in patients after AF ablation. Subjects will be randomized to OAC or WATCHMAN FLX. The duration of individual subject participation is expected to last approximately 36 months. Follow-up visits to occur at 3, 12, 24, and 36 months following randomization.

PARTIAL CRITERIA LIST/QUALIFICATIONS:

Inclusion:
- Underwent a prior catheter ablation procedure for non-valvular AF between 90 and 180 days prior to randomization (sequential) or is planning to have clinically indicated catheter ablation within 10 days of randomization (concomitant).
- The subject has a calculated CHA2DS2-VASc score of 2 or greater for males or 3 or greater for females.

Exclusion:
The subject requires long-term anticoagulation therapy for reasons other than AF-related stroke risk reduction, for example due to an underlying hypercoagulable state (i.e., even if the device is implanted, the subjects would not be eligible to discontinue OAC due to other medical conditions requiring chronic OAC therapy).
Title: Left atrial appendage closure for atrial fibrillation patients: updates on surgical and transcatheter device options

Speaker: Jacqueline Saw, MD, FRCPC, FACC, FAHA, FSCAI
Clinical Professor
Vancouver General Hospital

Date: September 16, 2019
Time: 7:00 - 8:00 AM
Location: Minneapolis Heart Institute Building, Suite 100, Learning Center

OBJECTIVES
At the completion of this activity, the participants should be able to:
1. Describe the epidemiology of atrial fibrillation and stroke.
2. Describe the guidelines indications and limitations for anticoagulation.
3. Identify the data, devices and indications for left atrial appendage closure.

ACCREDITATION

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Moderator(s)/Speaker(s)
Dr. Saw has disclosed the following relationships. Boston Scientific, Abbott Vascular, UBC-Division of Cardiology, AstraZeneca, Bayer and Sunovion in one or more of the following roles: Grant/research support, Consultant, Speaker’s Bureau and Honoraria.
Planning Committee
Dr. Alex Campbell, Jake Cohen, Jane Fox, Dr. Kevin Harris, Dr. Kasia Hryniewicz, Rebecca Lindberg, Amy McMeans, Dr. Michael Miedema, Dr. JoEllyn Moore, Pamela Morley, Dr. Scott Sharkey, Maia Hendel and Jolene Bell Makowesky have disclosed that they DO NOT have any real or apparent conflicts with any commercial interest as it relates to the planning of this activity/course. Dr. Mario Gössl has disclosed the following relationships – Edwards Life Sciences: Grant/Research Support; Abbott Vascular, Caisson: Consultant; Speaker’s Bureau: Edwards Lifesciences. Dr. David Hurrell has disclosed the following relationship – Boston Scientific: Chair, Clinical Events Committee.

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Signature: _______________________________________

My signature verifies that I have attended the above stated number of hours of the CME activity.

Allina Health - Learning & Development - 2925 Chicago Ave - MR 10701 - Minneapolis MN 55407
Left Atrial Appendage Closure: 
Current State of the Art and Future Directions

Jacqueline Saw MD, FRCPC, FACC, FAHA, FSCAI, FSCCT

Clinical Professor
Interventional Cardiology
Vancouver General Hospital
University of British Columbia

Disclosures

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company/Institution</th>
</tr>
</thead>
</table>
| Grant/Research Support                            | Canadian Institutes of Health Research, Heart & Stroke  
Foundation of Canada, National Institutes of Health, Michael  
Smith Foundation of Health Research, AstraZeneca, Boston  
Scientific, Abbott Vascular, Servier                  |
| Consulting Fees/Honoraria                         | Abbott Vascular, AstraZeneca, Sunovion, Bayer, Boston  
Scientific, Abiomed, Gore, Baylis, FEops              |
| Proctor/Preceptor                                 | Boston Scientific, Abbott Vascular                                                                      |
| Research Studies Leadership                       | LAAC: Canadian Watchman Study (PI), ASAP-TOO (Co-PI),  
ACP/Amulet Canadian PMR (Co-PI), Amulet PMR (CEC Chair)  
SCAD: Canadian SCAD & Genetics Study (PI), SAFER-SCAD  
(Co-PI), PRYME (PI)                                    |
Update on Surgical and Transcatheter Therapy: Overview

- Epidemiology of AF and stroke
- Guidelines indications and limitations with OAC for stroke prevention
- LAAC therapy rationale, history & timeline
- Surgical LAAC history and recent data
- Percutaneous LAAC: WATCHMAN indications, recent data and update
- Future directions: new devices & trials, minimalist approach
AF affects 1-2% general population

AF-related stroke risk & disability

5X increased risk of stroke for AF patients^2

1 in 6 strokes occur in patients with AF^3

~2X greater likelihood of stroke recurrence in AF patients (within 6 months)^4

AF-related Stroke

1.5X higher disability^**

2X higher mortality^**

70% result in death or permanent disability^h

*compared with stroke patients without AF

Stroke

#1 cause of adult disability worldwide^*

Visual Impairment* 
Aphasia*
Hemiparesis*
Unable to Walk Unassisted*
Employed Post-Stroke^2

Cognitive Deficits*
Depression*
Social Disability*
Bladder Incontinence*


Nonvalvular AF: Guidelines OAC Indication

- ACC/AHA 2019: CHA₂DS₂-VASc ≥2 men, ≥3 women
- ESC 2016: CHA₂DS₂-VASc ≥1*
- CCS 2016: age ≥65
  (or stroke/TIA, HTN, CHF, or DM)

*except for women with lone AF

NCDR PINNACLE Registry: 2008-2012

429,417 outpatients with AF in US

European Heart Journal 2016.
GARFIELD-AF Registry: 39,670 patients

Limitations with NOAC

Annual Major Bleeding Rate
UK Real-World OAC Discontinuation Rate

Design: Cohort study in Clinical Practice Research Datalink.
Setting: UK primary care.
Participants: 15,242 patients with NVAF newly prescribed apixaban, rivaroxaban, dabigatran or vitamin K antagonists (VKAs) between 1 December 2012 and 31 October 2014. 13,089 patients were OAC naïve.

Adherence to OACs (PDC ≥80%) within 1st 6mth follow-up, stratified by index medication (n=64,661)

<table>
<thead>
<tr>
<th>Adjusted Adherence</th>
<th>Apixaban (n=3900)</th>
<th>Dabigatran (n=10235)</th>
<th>Rivaroxaban (n=12336)</th>
<th>All NOACs (n=26471)</th>
<th>Warfarin (n=38190)</th>
<th>P value (all NOACs pooled vs warfarin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>62.5% (60.8-64.2)</td>
<td>57.3% (56.2-58.4)</td>
<td>59.5% (58.5-60.5)</td>
<td>58.9% (58.2-59.7)</td>
<td>49.9% (49.3-50.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS-VASc 0 or 1</td>
<td>51.2% (46.3-56.1)</td>
<td>41.4% (39.0-43.7)</td>
<td>44.4% (42.1-46.7)</td>
<td>43.7% (42.1-45.2)</td>
<td>37.8% (35.9-39.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS-VASc 2 or 3</td>
<td>62.4% (59.9-65.2)</td>
<td>58.3% (56.6-60.0)</td>
<td>60.1% (58.6-61.6)</td>
<td>59.6% (58.5-60.6)</td>
<td>48.3% (47.3-49.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS-VASc ≥4</td>
<td>64.4% (62.2-66.5)</td>
<td>59.5% (58.0-61.0)</td>
<td>61.7% (60.3-63.0)</td>
<td>61.1% (60.2-62.1)</td>
<td>52.8% (52.1-53.5)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Left Atrial Appendage

- Remnant of embryonic LA
- Complex & highly variable anatomy
- Usually long, tubular, multi-lobed
- Excessive trabeculations from pectinate muscle
- Extends over the AV groove & LV surface
- Functions: decompression chamber, ANF storage

Left Atrial Appendage

- Long, blind-ended pouch, excessive trabeculations, cause stasis

Functional Changes
- Decreased contractility
- Decreased velocity

Structural Remodeling
- Enlargement (volume & surface area)
- Endocardial fibroelastosis
- Smoother surface

Virchow’s Triad
- Endothelial or endocardial damage
- Blood stasis
- Altered hemostasis

Thrombus Formation

<table>
<thead>
<tr>
<th>Setting</th>
<th>Thrombi in LAA and atrium</th>
<th>Found LAA</th>
<th>Found in left atrium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>LAA and atrium</td>
<td>67</td>
<td>66</td>
<td>99%</td>
</tr>
<tr>
<td>TEE</td>
<td>35</td>
<td>34</td>
<td>97%</td>
</tr>
<tr>
<td>Autopsy</td>
<td>47</td>
<td>35</td>
<td>74%</td>
</tr>
<tr>
<td>TEE</td>
<td>4</td>
<td>2</td>
<td>50%</td>
</tr>
<tr>
<td>TEE &amp; operation</td>
<td>13</td>
<td>12</td>
<td>92%</td>
</tr>
<tr>
<td>SPAF III &amp; TEE</td>
<td>11</td>
<td>8</td>
<td>73%</td>
</tr>
<tr>
<td>TEE</td>
<td>20</td>
<td>19</td>
<td>95%</td>
</tr>
<tr>
<td>TEE</td>
<td>19</td>
<td>19</td>
<td>100%</td>
</tr>
<tr>
<td>TEE</td>
<td>6</td>
<td>6</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>222</td>
<td>201</td>
<td>91%</td>
</tr>
</tbody>
</table>

LAA Surgical Excision/Exclusion: Since 1949

<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Country</th>
<th>No. Studied</th>
<th>Method of Closure</th>
<th>Effect of LAA Closure on Stroke Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katz, 2000 [30]</td>
<td>USA</td>
<td>50</td>
<td>Endocardial suture</td>
<td>64</td>
</tr>
<tr>
<td>Garcia-Fernandez, 2000 [31]</td>
<td>Spain</td>
<td>205</td>
<td>Endocardial suture</td>
<td>Positive</td>
</tr>
<tr>
<td>Bande, 2003 [38]</td>
<td>Japan</td>
<td>812</td>
<td>Endocardial suture</td>
<td>90</td>
</tr>
<tr>
<td>Blackshear, 2003 [45]</td>
<td>USA</td>
<td>15</td>
<td>Thoracoscopic epicardial pursesting</td>
<td>Negative</td>
</tr>
<tr>
<td>Penne, 2003 [40]</td>
<td>France</td>
<td>30</td>
<td>Endocardial</td>
<td>93%</td>
</tr>
<tr>
<td>Schneider, 2005 [41]</td>
<td>Germany</td>
<td>6</td>
<td>Excision</td>
<td>None</td>
</tr>
<tr>
<td>Healey, 2005 [28]</td>
<td>Canada</td>
<td>77</td>
<td>Epicardial suture</td>
<td>Positive</td>
</tr>
<tr>
<td>Kandarian, 2008 [29]</td>
<td>USA</td>
<td>137</td>
<td>Stapler</td>
<td>Positive trend</td>
</tr>
<tr>
<td>Rakhitaya, 2008 [33]</td>
<td>Germany</td>
<td>259</td>
<td>Suture exclusion</td>
<td>Positive</td>
</tr>
</tbody>
</table>

- Requires open heart surgery
- Varying approaches & success rates
- Unclear clinical benefits
- Incomplete closure associated with thrombus & stroke

Cleveland Clinic: N=2546, 137 had post-op TEE

Low success rate with exclusion (defined as remnant LAA cavity (stump >1cm) or persistent flow
Surgical LAA Closure Complications

**Table 5.2 Complications of left atrial appendage occlusion**

<table>
<thead>
<tr>
<th>Major complications</th>
<th>Minor complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oclusion or injury to circumflex artery</td>
<td>• Arrhythmias</td>
</tr>
<tr>
<td>• Left superior pulmonary vein injury</td>
<td>• Decreased ANP production leading to impaired fluid balance</td>
</tr>
<tr>
<td>• Myocardial tears</td>
<td>• Minor bleeding from the occlusion site</td>
</tr>
<tr>
<td>• Major bleeding from the occlusion site (requiring transfusions and/or surgery)</td>
<td></td>
</tr>
<tr>
<td>• Incomplete LAA occlusion leading to increased risk of thrombus formation</td>
<td></td>
</tr>
<tr>
<td>• Thromboembolism (stroke)</td>
<td></td>
</tr>
</tbody>
</table>


Impact of Left Atrial Appendage Closure During Cardiac Surgery on the Occurrence of Early Postoperative Atrial Fibrillation, Stroke, and Mortality

**A Propensity Score–Matched Analysis of 10633 Patients**

**METHODS:** Of 10633 adults who underwent coronary artery bypass grafting and valve surgery between January 2000 and December 2005, 9792 patients with complete baseline characteristics, surgery procedure, and followup data were included in this analysis. A propensity score–matching analysis based on 28 pretreatment covariates was performed and 461 matching pairs were derived and analyzed to estimate the association of LAA closure with early postoperative atrial fibrillation (POAF) (atrial fibrillation ≤30 days of surgery), ischemic stroke, and mortality.

**RESULTS:** In the propensity-matched cohort, the overall incidence of POAF was 53.9%. In this group, the rate of early POAF among the patients who underwent LAA closure was 68.6% versus 31.9% for those who did not undergo the procedure (P<0.001). LAA closure was independently associated with an increased risk of early POAF (adjusted odds ratio: 3.88; 95% confidence interval: 2.89–5.20), but did not significantly influence the risk of stroke (adjusted hazard ratio: 1.07; 95% confidence interval: 0.72–1.58) or mortality (adjusted hazard ratio: 0.92; 95% confidence interval: 0.75–1.13).

**CONCLUSIONS:** After adjustment for treatment allocation bias, LAA closure during routine cardiac surgery was significantly associated with an increased risk of early POAF, but it did not influence the risk of stroke or mortality. It remains uncertain whether prophylactic exclusion of the LAA is warranted for stroke prevention during non–atrial fibrillation-related cardiac surgery.

- Prospectively Mayo Clinic Cardiovascular Surgery Database for CABG and valve surgery Jan2000-Dec2005
- Propensity-matched 461 pts 1:1 with LAAC (n=469) and no LAAC (n=9323)
- 48% had baseline AF
- Excision 2.3%, ligation 97.7%
- LAAC increased post-op AF, did not affect stroke/mortality
**JAMA. 2018;319(4):365‐374.**

**Association Between Left Atrial Appendage Occlusion and Readmission for Thromboembolism Among Patients With Atrial Fibrillation Undergoing Concomitant Cardiac Surgery**

- 3892 S-LAAO vs. 6632 no S-LAAO

**JAMA. 2018;319(20):2116‐2126.**

**Association of Surgical Left Atrial Appendage Occlusion With Subsequent Stroke and Mortality Among Patients Undergoing Cardiac Surgery**

- 4374/75782 (5.8%) had surgical LAAO (1/4 did not have baseline AF)
- Unknown exclusion/excision, closure success
- 8590 propensity score‐matched pts
- Mean FU 2.1yr
- LAAO lower risk of stroke (HR 0.73, p=0.03) and mortality (HR 0.71, p<0.001)
- Interaction between LAAO and prior AF not statistically significant
- Risk of AF higher in LAAO pt without baseline AF (HR 1.46, p<0.001)
Meta-Analysis Evaluating Outcomes of Surgical Left Atrial Appendage Occlusion During Cardiac Surgery

Abdisamad M. Ibrahim, MD MSc, Nitin Tandan, MD, Cameron Koester, DO, Mohammad Al-Akchar, MD, Bishal Bhandari, DO, Albert Bocchway, PhD, Junama Abdelkarim, MD, Ruby Maini, MD, and Mohamed Labed, MD

Surgical left atrial appendage occlusion (SLAAO) has become a common procedure performed in patients undergoing cardiac surgery; however, evidence to support this procedure remains inconclusive. This meta-analysis aims to assess the efficacy of SLAAO in terms of ischemic stroke, postoperative atrial fibrillation, and all-cause mortality. A thorough literature search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. We identified 19 relevant studies for our meta-analysis. It included 6,729 patients who underwent SLAAO and 6,574 who did not undergo LAAC. In terms of ischemic stroke, the SLAAO cohort had a lower event (pooled odds ratio [OR] 0.665 [0.518 to 0.829], p = 0.004) compared with the non-SLAAO cohort. SLAAO cohort also had lower events of all-cause mortality (pooled OR 0.74 [95% confidence interval 0.55 to 0.99], p = 0.040) when compared with the non-SLAAO cohort.

Adding left atrial appendage closure to open heart surgery provides protection from ischemic brain injury six years after surgery independently of atrial fibrillation history: the LAACS randomized study

Jesper Park-Hansen1,2, Susanne J.V. Holme3, Ahmadjon Imrulhamenedo4, Christian L. Caranza2, Anders M. Greve2, Gina Al-Fam2, Robert G. C. Ritt2, Brian Nilsson2, Johan S.R. Clausen2, Anne S. Norskov2, Christina R. Kruse2, Steff Rostrup5 and Helena Dominguez5,6

Study design
From August 2010 to September 2013, we conducted a prospective, randomized, open label study on patients scheduled for open heart surgery to receive either concomitant LAACS or standard care. The LAACS study is registered at clinicaltrial.gov (NCT02378116). The study was initiated at the Department of Thoracic Surgery, University Hospital of Gentofte, Denmark.

The study protocol recommended double closure with both purse string and running suture, although this closure method was not mandatory. Patients were invited to pre-surgery magnetic resonance imaging (MRI) scan (MRI-0) whenever possible. Immediately after discharge, all patients were invited for a post-operative baseline brain MRI scan (MRI-1) scheduled between 2 and 4 weeks after discharge and a follow-up MRI (MRI-2) performed at least 6 months after surgery.

187 pts randomized to LAAC versus not

Table 2: Proportion of patients meeting endpoints according to randomized left atrial appendage closure, stratified by use of anti-coagulants

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Not closed</th>
<th>Closed</th>
<th>Hazard ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary events\a</td>
<td>14 (16.1%)</td>
<td>5 (5.0%)</td>
<td>0.63 [0.36–0.91]</td>
<td>0.0396</td>
</tr>
<tr>
<td>Clinical stroke\a</td>
<td>8 (10.0%)</td>
<td>3 (3.0%)</td>
<td>0.63 [0.36–0.91]</td>
<td>0.0763</td>
</tr>
<tr>
<td>Death</td>
<td>12 (14.0%)</td>
<td>12 (11.9%)</td>
<td>0.85 [0.43–1.69]</td>
<td>0.6562</td>
</tr>
</tbody>
</table>

\aDefined as first of postoperative symptomatic ischemic stroke, transient ischemic attack or imaging evidence of new silent infarct

only 40% had both MRI
AtriClip LAA Exclusion System

- FDA 510(k) approval
- Sizes: 35, 40, 45, 50mm
- 2 parallel nitinol tubes covered with knit-braided polyester sheath
- applies uniform pressure on a beating heart, & redeployment
- clip is applied to the base of LAA (not affected by atypical morphologies)
- can be applied with concomitant cardiac surgery or thoracoscopic procedures

**IV. Indications For Use**

The AtriClip LAA Exclusion System is indicated for the exclusion of the left atrial appendage, under direct visualization, in conjunction with other cardiac surgical procedures.

Direct visualization, in this context, requires that the surgeon is able to see the heart directly, with or without assistance from a camera, endoscope, etc., or any other viewing technologies.

**Epicardial left atrial appendage AtriClip occlusion reduces the incidence of stroke in patients with atrial fibrillation undergoing cardiac surgery**

A total of 291 AtriClip devices were deployed epicardially in patients (mean CHA2DS2-VASc Score: 3.1 ± 1.5) undergoing open-heart surgery (including isolated coronary artery bypass grafting, valve, or combined procedures) comprising of forty patients from a first-in-man device trial (NCT00567515) and 251 patients from a consecutive institutional registry thereafter. In all patients (n=291), the LAA was successfully excluded and overall mean follow-up (FU), was 36 ± 23 months (range: 1-97 months). No device-related complications were detected throughout the FU period. Long-term imaging workup (computed tomography) in selected patients ≥3 years post-implant (range: 5.1-81 years) disclosed complete LAA occlusion with no signs of residual reperfusion or significant LAA stumps. Subgroup analysis of patients with discontinued OAC during FU (n = 116) showed a relative risk reduction of 87.5% with an observed ischemic stroke-rate of 0.3/100 patient-years compared with what would have been expected in a group of patients with similar CHA2DS2-VASc scores (expected rate of 2.0/100 patient-years). No strokes occurred in the subgroup with OAC.

- AtriClip successfully implanted in 291pt undergoing open-heart sx
- No device-related procedural complications
- Intraop TEE confirmed complete LAA closure without stump >1cm
- Majority had AF (only 2.4% no AF), 65.5% discharged on OAC
- Mean FU 36mth: no device-related complication

43 patients had CCTA post (mean 7yr post-implant):
- 31 (72%) no residual stump
- 11 (26%) had residual stump <10mm
- 1 (2%) had residual stump >10mm depth

RESULTS: The LAA was successfully occluded in all 43 patients (100%) as confirmed by intraoperative transesophageal echocardiography and CTA imaging with a mean follow-up duration of 7.1 ± 0.8 years post-implant. The absence of blood flow in the excluded LAA was confirmed in all cases. In 31 of 43 patients (72%), no residual stump (0 mm) was observed creating a smooth endocardial surface. CTA revealed residual LAA stumps in 11/43 patients (26%) with a length <10 mm and a significant residual stump with a depth of >10 mm (12 mm) in 1 patient (2%). The mean length, width, and depth of the residual stumps were 5.8 ± 2.1, 4.4 ± 1.2 and 7.3 ± 2.3 mm, respectively.

CONCLUSIONS: This study investigated the incidence of residual stump formation (>10 mm) after LAA closure with the Atriclip device based on CTA imaging obtained during short- and long-term follow-up. While no LAA stump was detectable in the majority of patients, a non-significant LAA stump (<10 mm) was present in 26% of cases, indicating a favorable LAA occlusion profile for the Atriclip device. However, although a LAA stump length <10 mm is currently considered clinically safe, this definition needs further attention in future studies with regards to its potential clinical implications.
Outcomes of left atrial appendage occlusion using the AtriClip device: a systematic review

Conor Toale @, Gerard J. Fitzmaurice @, Donna Eaton, Jonathan Lyne and Karen C. Redmond**

- 11 studies, 922 patients
- 93.9% had history of AF
- Approach: 4 studies thoracoscopically, 4 studies median sternotomy, 2 studies mini-thoracotomy
- Complete LAAO achieved in 902/922 pts (97.8%)
- Lower success rate thoracoscopic (95.3% vs 99.2%, p=0.0002)
- No device-related adverse events were reported
- Stroke or TIA post-clipping provided ranged from 0.2 to 1.5/100pt-yrs
- 477/798 patients (59.7%) stopped OAC on FU

AtriClip implant appears safe (1% pericardial effusion, tachyarrhythmia, atelectasis)

Unclear role of OAC post-AtriClip

Limited studies on FU success

No RCT on efficacy for prevention of thromboembolism

Rationale and design of the Left Atrial Appendage Occlusion Study (LAAOS) III


Background: Occlusion of the left atrial appendage (LAA) is a promising approach to stroke prevention in atrial fibrillation (AF). However, evidence of its efficacy and safety to date is lacking. We herein describe the rationale and design of a definitive LAA occlusion trial in cardiac surgical patients with AF.

Methods: We plan to randomize 4,700 patients with AF in whom on-pump cardiac surgical procedure is planned to undergo LAA occlusion or no LAA occlusion. The primary outcome is the first occurrence of stroke or systemic arterial embolism over a mean follow-up of four years. Other outcomes include total mortality, operative safety outcomes (chest tube output in the first post-operative 24 hours, rate of post-operative re-exploration for bleeding in the first 48 hours post-surgery and 30-day mortality), re-hospitalization for heart failure, major bleed, and myocardial infarction.

Results: Left Atrial Appendage Occlusion Study (LAAOS) III is funded by the Canadian Institutes of Health Research (CIHR), the Canadian Network and Centre for Trials Internationally, and the McMaster University Surgical Associates. As of September 9, 2013, 162 patients have been recruited into the study.

Conclusions: LAAOS III will be the largest trial to explore the efficacy of LAA occlusion for stroke prevention. Its results will lead to a better understanding of stroke in AF and the safety and efficacy of surgical LAA occlusion.

- Mode of LAAC at discretion of surgeon
- OAC is recommended after LAAC
- Finished enrolment, mean FU 4yr
2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Recommendations for occlusion or exclusion of the left atrial appendage

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alter surgical occlusion or exclusion of the LAA when transesophageal echocardiography demonstrates a large, leftward appendage with a subvalvular interatrial sulcus (34, 37)</td>
<td>I A</td>
<td>B</td>
<td>461, 462</td>
</tr>
<tr>
<td>LAA occlusion may be considered for stroke prevention in patients with AF and contra-indications for long-term antiplatelet treatment (e.g. those with a previous life-threatening bleed without a reversible cause).</td>
<td>IIb A</td>
<td>B</td>
<td>449, 451, 454</td>
</tr>
<tr>
<td>Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing cardiac surgery.</td>
<td>IIb A</td>
<td>B</td>
<td>463</td>
</tr>
</tbody>
</table>

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

4.4.1. Percutaneous Approaches to Oclude the LAA

1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (54.4.1.1–54.4.1.5).

   - NEW: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.

4.4.2. Cardiac Surgery—LAA Occlusion/Excision

1. Surgical occlusion of the LAA may be considered in patients with AF undergoing cardiac surgery (54.4.2.1), as a component of an overall heart team approach to the management of AF.

   - MODIFIED: LOE was updated from C to B-NR because of new evidence.

Percutaneous LAAC

**TABLE 1 LAA Closure Devices**

<table>
<thead>
<tr>
<th>Device Name</th>
<th>Company</th>
<th>Design</th>
<th>Device Sizes</th>
<th>Approval Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLAATO</td>
<td>Atriva Medical Inc.</td>
<td>Single-lumen catheter, nitinol wire, aPTFE membrane, hooks</td>
<td>16, 18, 20, 26, 29, and 32 mm (14-F sheath)</td>
<td>Removed from market</td>
</tr>
<tr>
<td>Watchman</td>
<td>Boston Scientific</td>
<td>Single-lumen catheter, nitinol frame, PET membrane, hooks</td>
<td>21, 24, 27, 30, and 33 mm (16-F sheath)</td>
<td>FDA approval, CE mark</td>
</tr>
<tr>
<td>ACP</td>
<td>St. Jude Medical</td>
<td>Lobe and disk (polymer mesh in both), nitinol mesh structure, stabilizing wires</td>
<td>16, 18, 20, 21, 26, 28, and 30 mm (9, 10, 13-F sheaths)</td>
<td>CE mark</td>
</tr>
<tr>
<td>Amulet</td>
<td>St. Jude Medical</td>
<td>Lobe and disk (polymer mesh in both), nitinol mesh structure, stabilizing wires</td>
<td>16, 18, 20, 22, 25, 28, 31, and 34 mm (12- and 14-F sheaths)</td>
<td>CE mark</td>
</tr>
<tr>
<td>WaveCrest</td>
<td>Cordis Medical</td>
<td>Single-lumen catheter, nitinol frame, polyurethane foam and aPTFE membrane, retrievable anchors</td>
<td>22, 27, and 32 mm</td>
<td>CE mark</td>
</tr>
<tr>
<td>Occluder LAA</td>
<td>Occlutech</td>
<td>Single-lumen catheter, nitinol wire mesh, stabilizing loops</td>
<td>16, 18, 21, 26, 30, 33, 36, and 39 mm (13- and 14-F sheaths)</td>
<td>CE mark</td>
</tr>
<tr>
<td>LAAmbre</td>
<td>Lifetech</td>
<td>Lobe and disk, nitinol, PET membrane, distal barbs anchors</td>
<td>16 to 36 mm (7- to 10-F sheaths)</td>
<td>CE mark</td>
</tr>
<tr>
<td>Sideris Transcatheter Patch</td>
<td>Custom Medical Devices</td>
<td>Frameless detachable latex balloon covered with polyurethane</td>
<td>Clinical trial evaluation</td>
<td></td>
</tr>
<tr>
<td>PFM</td>
<td>PFM Medical</td>
<td>Dual disk (distal anchors, variable middle connector, proximal disk), nitinol frame</td>
<td>(B- and S-F sheaths)</td>
<td>Pre-clinical trial evaluation</td>
</tr>
<tr>
<td>UltraSpect</td>
<td>Cardia</td>
<td>Lobe and disk, nitinol frame, balloon covering, distal anchors</td>
<td>16, 20, 24, 28, and 32 mm (10- and 12-F sheaths)</td>
<td>CE mark</td>
</tr>
</tbody>
</table>

**Epidermal Devices**

<table>
<thead>
<tr>
<th>Device Name</th>
<th>Company</th>
<th>Design</th>
<th>Device Sizes</th>
<th>Approval Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lariat</td>
<td>SentreHeart</td>
<td>Endocardial and epicardial approach guided by magnetic-assisted snare over balloon in LAA</td>
<td>14-F epicardial sheath</td>
<td>FDA approval, CE mark</td>
</tr>
<tr>
<td>AfriClip</td>
<td>Atriga</td>
<td>Surgical approach parallel clip with polyester mesh</td>
<td>35, 40, 45, and 50 mm</td>
<td>FDA approval, CE mark</td>
</tr>
<tr>
<td>Adeq</td>
<td>AEGIS Medical Innovations</td>
<td>Epicardial subepicardial approach, electrodes guide navigation to LAA and tissue capture</td>
<td>Clinical trial evaluation</td>
<td></td>
</tr>
<tr>
<td>Cardiablate</td>
<td>Medtronic</td>
<td>Epicardial approach, silicone band covered by polyester fabric</td>
<td>Pre-clinical trial evaluation</td>
<td></td>
</tr>
</tbody>
</table>
WATCHMAN: Boston Scientific

CE Mark 2005, FDA Mar 2015, >80 countries, >100,000 implants

- Nitinol Frame 5 sizes
- Delivered via 14Fr sheaths
- Repositionable & retrievable
- Radially expands to maintain position in LAA

1st implant
Aug 2002

- 10 active fixation anchors
- Designed to stabilize device

- 160um polyethyl terephthalate (PET) membrane
- Promote healing at 45 days

WATCHMAN™ Clinical Timeline

More than 3,000 patients and nearly 7,000 patient-years of follow-up

2002 – Pilot nonrandomized Feasibility and Safety
2005 – PROTECT AF Randomized Comparison: warfarin
2008 – CAP Registry non-randomized Add'l patients and follow-up
2009 – ASAP non-randomized Patients Contra-indicated to warfarin
* Not US indication
2010 – PREVAIL Randomized Comparison: warfarin
2012 – CAP2 Registry Non-Randomized Add'l patients and follow-up
2013 EWOLUTION, WASP Registries non-randomized Real-world, All comers
2016 NCDR LAAO Registry Post-approval statistical analysis
2017 ASAP TOO Randomized US Indication Expansion Worldwide study

Mar 2015 FDA Approval
Apr 2009 FDA Panel #1
Oct 2014 FDA Panel #3
Dec 2013 FDA Panel #2
**Procedural Success**

Implant success defined as deployment and release of the device into the LAA; no leak ≥ 5 mm

* The EWOLUTION Registry is a European prospective registry which reflects CE Mark indications for use which differ from the FDA indications for use.


**Device Safety Endpoint Met**

Proc/Device Rel. Safety AE w/in 7 days

Procedure/device-related safety events to 7d: perforation, tamponade, ischemic stroke, device embolization, vascular complications

* The EWOLUTION Registry is a European prospective registry which reflects CE Mark indications for use which differ from the FDA indications for use.

Temporal Trends Procedural Complications: Watchman


WM: Major Procedural Complication Rates


| TABLE 4 Comparison of Procedural Complications Across Watchman Studies |
|-------------------------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| PROTECT-AF | PREVAIL | CAP | CAP2 | EWOLUTION | Post-FDA Approval | Aggregate Data* |
| Pericardial tamponade | 20 (4.3) | 5 (1.9) | 8 (1.4) | 11 (1.9) | 3 (0.29) | 39 (1.02) | 86 (1.28) |
| Treated with pericardiocentesis | 13 (2.8) | 4 (1.5) | 7 (1.2) | N/A | 2 (0.20) | 24 (0.63) | 67% |
| Treated surgically | 7 (1.5) | 1 (0.4) | 1 (0.2) | N/A | 1 (0.10) | 12 (0.31) | 29% |
| Resulted in death | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (0.078) | 4% |
| Pericardial effusion, no intervention | 4 (0.9) | 0 (0) | 5 (0.9) | 3 (0.5) | 4 (0.39) | 11 (0.29) | 27 (0.40) |
| Procedure-related stroke | 5 (1.15) | 1 (0.37) | 0 (0) | 2 (0.35) | 1 (0.10) | 3 (0.078) | 12 (0.18) |
| Device embolization | 3 (0.6) | 2 (0.7) | 1 (0.2) | 0 (0) | 2 (0.20) | 9 (0.24) | 17 (0.25) |
| Removed percutaneously | 1 | 0 | 0 | 0 | 1 | 3 | 29% |
| Removed surgically | 2 | 2 | 1 | 0 | 1 | 6 | 71% |
| Death | | | | | | | |
| Procedure-related mortality | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0.1) | 3 (0.078) | 4 (0.06) |
| Additional mortality within 7 days | 0 (0) | 0 (0) | 0 (0) | 1 (0.17) | 3 (0.29) | 1 (0.028) | 5 (0.07) |

Favorable Procedural Safety Profile:
Major Procedural Complications Across WATCHMAN Studies

Clinical Trial Experience

Post Approval Experience

Complication Rates

PROTECT AF & PREVAIL: 5yr Results

TABLE 3 Efficacy Rates at 5 Years (2:1 Randomization)

<table>
<thead>
<tr>
<th></th>
<th>PROTECT AF Subjects</th>
<th>PREVAIL-Only Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Device Group (n = 463)</td>
<td>Control Group (n = 244)</td>
</tr>
<tr>
<td>No. of Events</td>
<td>Rate*</td>
<td>No. of Events</td>
</tr>
<tr>
<td>Primary efficacy: stroke/SE/CV death</td>
<td>40/1,787.7 2.24</td>
<td>34/929.4 3.66</td>
</tr>
<tr>
<td>All stroke</td>
<td>26/1,781.7 1.46</td>
<td>20/929.4 2.15</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>24/1,781.7 1.35</td>
<td>10/932.8 1.07</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>3/1,837.7 0.16</td>
<td>10/945.6 1.06</td>
</tr>
<tr>
<td>Systemic embolism</td>
<td>3/1,837.1 0.16</td>
<td>0  N/A</td>
</tr>
<tr>
<td>CV/unexplained death</td>
<td>19/1,843.2 1.03</td>
<td>22/948.9 2.32</td>
</tr>
</tbody>
</table>

Anticoagulation Regimen

- Implant to 6 weeks
  - Warfarin (INR 2-3) for 6 weeks
  - Aspirin (81 – 325 mg)
  - Clopidogrel (75 mg)
  - Aspirin (81 – 325 mg)
  - After 6 months
    - Aspirin (81 – 325 mg)

Warfarin-eligible Patients: 2:1 WATCHMAN:Warfarin
Meta-analysis: PROTECT AF & PREVAIL (5yr, N=1114)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke or SE</td>
<td>0.82</td>
<td>0.3</td>
</tr>
<tr>
<td>Ischemic stroke or SE</td>
<td>0.96</td>
<td>0.9</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>1.7</td>
<td>0.08</td>
</tr>
<tr>
<td>Ischemic stroke or SE &gt;7 days</td>
<td>0.2</td>
<td>0.0022</td>
</tr>
<tr>
<td>Non-Disabling Stroke</td>
<td>1.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Disabling/Fatal Stroke (MRS change of ≥2)</td>
<td>0.45</td>
<td>0.03</td>
</tr>
<tr>
<td>CV/unexplained death</td>
<td>0.59</td>
<td>0.03</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.73</td>
<td>0.04</td>
</tr>
<tr>
<td>Major bleed, all</td>
<td>0.91</td>
<td>0.6</td>
</tr>
<tr>
<td>Major bleeding, non procedure-related</td>
<td>0.48</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

The ischemic stroke rates with nonvalvular AF as a function of baseline CHADS-VASc score
Watchman Approval in US March 2015

**FDA Approval**
- WATCHMAN is indicated to reduce the risk of thromboembolism from the LAA in patients with non-valvular AF who are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores,
- Are deemed by their physicians to be suitable for warfarin; and have an appropriate rationale to seek a non-pharmacologic alternative to warfarin

**CMS Coverage Determination**
- CHADS2 ≥2 or CHADS-VASc ≥3
- Formal shared decision making with independent non-interventional physician
- Suitable for short-term warfarin, but unable to take long-term OAC
- Patient enrolled in prospective national audited registry, or
- FDA-approved RCT comparing to OMT (primary endpoint stroke/SE)

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**Post-Approval U.S. Experience With Left Atrial Appendage Closure for Stroke Prevention in Atrial Fibrillation**

*Vivek Y. Reddy, MD, a Douglas N. Gibson, MD, b Sibhal Kar, MD, a William O’Neill, MD, a Shephal K. Doshi, MD, a Rodney P. Hoston, MD, a Maurice Ruchbinder, MD, a Nicole T. Gordon, BSEE, a David R. Holmes, MD a*

- After US Watchman approval: from Mar 2015 to May 2016
- 3822 consecutive patients underwent Watchman implant
- 382 physicians, 169 US centers
- 50% procedures performed by newly trained operators
- Each implanted attended by Watchman clinical specialist
- Procedural details recorded and events reported to manufacturer

<table>
<thead>
<tr>
<th>Complications</th>
<th>Post-FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial Tamponade</td>
<td>39 (1.02%)</td>
</tr>
<tr>
<td>Treated with Pericardiocentesis</td>
<td>24 (0.63%)</td>
</tr>
<tr>
<td>Treated Surgically</td>
<td>12 (0.31%)</td>
</tr>
<tr>
<td>Resulted in Death</td>
<td>3 (0.078%)</td>
</tr>
<tr>
<td>Pericardial Effusion – No Intervention</td>
<td>11 (0.29%)</td>
</tr>
<tr>
<td>Procedure-Related Stroke</td>
<td>3 (0.078%)</td>
</tr>
<tr>
<td>Device Embolization</td>
<td>9 (0.24%)</td>
</tr>
<tr>
<td>Removed Percutaneously</td>
<td>3</td>
</tr>
<tr>
<td>Removed Surgically</td>
<td>6</td>
</tr>
<tr>
<td>Additional Mortality within 7 days</td>
<td>1 (0.026%)</td>
</tr>
</tbody>
</table>

Currently: ~600 implant sites, ~50,000 implants in USA

### WATCHMAN NESTed PAS

- Data acquired from the LAAO Registry within the NCDR
  - Pre-procedure, implant, 45 days, 6 months, 12 months and 24 months post-procedure
  - Years 3-5 data will be provided through a linkage to CMS
- 1000 patient cohort data collected 4/16-11/16
- 132 sites reported data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PROTECT</th>
<th>CAP</th>
<th>PREVAIL</th>
<th>CAP2</th>
<th>EVOLUTION</th>
<th>NESTed</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHADS² Score</td>
<td>N=707</td>
<td>N=566</td>
<td>N=407</td>
<td>N=79</td>
<td>N=1025</td>
<td>N=270</td>
</tr>
<tr>
<td></td>
<td>2.2 ± 1.2</td>
<td>2.4 ± 1.2</td>
<td>2.6 ± 1.0</td>
<td>2.7 ± 1.1</td>
<td>2.8 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>CHA²DS²-VASc</td>
<td>3.4 ± 1.5</td>
<td>3.9 ± 1.5</td>
<td>4.0 ± 1.1</td>
<td>4.5 ± 1.3</td>
<td>4.5 ± 1.6</td>
<td></td>
</tr>
<tr>
<td>HAS-BLED</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>2.4 ± 1.2</td>
<td></td>
</tr>
</tbody>
</table>

Primary safety endpoint (within 7d or hospital discharge): all-cause death, ischemic stroke, systemic embolism, device or procedure related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair.

Presented at ACC 2018
Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry

Lucas V.A. Boersma1, Boris Schmidt1, Timothy R. Betts1, Horst Sievert1, Corrado Tamburino2, Emmanuel Teiger3, Evgeny Pokushalov4, Stephan Kiechel5, Thomas Schmitt6, Kenneth M. Stein7 and Martin W. Bergmann8, on behalf of the EWOLUTION investigators

- Prospective real-world registry (N=1021): 47 centers in Europe, Russia, Middle East, F/U 3mth
- 61.8% ineligible for OAC (38.7% prior major bleed or predisposition to bleed)
- DAPT used in 59.4% post-implant (OAC 27%)

**EWOLUTION:** Annual Stroke & Bleeding Rates

- Prospective real-world registry (N=1021): 47 centers in Europe, Russia, Middle East, F/U 3mth
- 61.8% ineligible for OAC (38.7% prior major bleed or predisposition to bleed)
- DAPT used in 59.4% post-implant (OAC 27%)

---

**Table I** Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Summary statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not eligible for OAC</td>
<td>61.8% (627/1021)</td>
</tr>
<tr>
<td>Age at time of consent (years)</td>
<td>73 (79, 94)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>75 (79, 94)</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>50.8% (519/1021)</td>
</tr>
<tr>
<td>Female gender</td>
<td>40.1% (409/1021)</td>
</tr>
<tr>
<td>History of TIA</td>
<td>10.7% (108/1014)</td>
</tr>
<tr>
<td>History of ischemic stroke</td>
<td>19.7% (200/1014)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>34.2% (347/1014)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>81.7% (628/1014)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 62% (639/1021)</td>
</tr>
<tr>
<td>Female 38% (382/1021)</td>
<td></td>
</tr>
</tbody>
</table>

**Diabetes**

- Type I: 22.3% (227/1014)
- Type II: 26.3% (267/1014)
- Previous hemorrhagic stroke: 15.6% (152/1014)
- Vascular disease: 41.9% (423/1014)
- Abnormal renal function: 18.4% (184/1014)
- Abnormal liver function: 4.2% (42/1014)
- History of major bleeding: 31.2% (316/1014)
- Prior major bleeding or predisposition to bleeding: 38.7% (387/1014)
- Labile INRs: 17.0% (172/1014)
- Concomitant use of drugs: 27.8% (282/1014)
- Alcohol abuse: 4.2% (42/1014)

**Post-implant Antithrombotic**

- SAPT: 6%
- DAPT: 27%
- none: 60%
- OAC: 7%

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**EWOLUTION:**
2-Year Follow-Up

Evaluating Real-World Clinical Outcomes in Atrial Fibrillation Patients Receiving the WATCHMAN Left Atrial Appendage Closure Technology
Final 2-Year Outcome Data of the EWOLUTION Trial Focusing on History of Stroke and Hemorrhage

**EWOLUTION Subgroup: 1yr Stroke & Bleeding Rates**

**ACP**
Abbott Vascular

**DESIGN:** Non-randomized, single-arm, multi-center clinical evaluation of the ACP in non-rheumatic AF patients

- Technical success 97.2%
- Annual stroke 2.3% (RRR59%)  
- Annual major bleed 2.1% (RRR61%)
- Device embolization 1%
- TEE F/U 632/1001 pt
- Any leak 11.6% (leak >3mm: 1.9%)
- Thrombus: 28/632 (4.4%) – no CVA

**HASBLED 3.1**
CHADS2=2.8
CHADS-VASc 4.5
Mean DAPT 3.8mth

**Left atrial appendage occlusion for stroke prevention in atrial fibrillation: multicentre experience with the AMPLATZER Cardiac Plug**

**DESIGN:** Non-randomized, single-arm, multi-center clinical evaluation of the ACP in non-rheumatic AF patients

- 1053 consecutive patients from 22 clinical sites in Europe and Canada, treated between December 2008 and November 2013.
- 1047 patients in study
- 1019 patients in study
- 1001 patients in study
- 6 pts missing data
- 28 pts not implanted
- 18 pts lost to F/U
- Stroke risk evaluation (predicted vs actual)
- Bleeding risk evaluation (predicted vs actual)

Amulet  Abbott Vascular

CE Mark Jan 2013

- Wider lobe
- More stabilizing wires
- Stiffer stabilizing wires
- Larger disc diameter
- Longer waist length
- Larger sizes (34mm)
- Pre-loaded
- Recessed endscrew

<table>
<thead>
<tr>
<th>Feature</th>
<th>Amulet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sizes (mm)</td>
<td>16 18 20 22 25 28 31 34</td>
</tr>
<tr>
<td>Disc Diameter</td>
<td>Lobe + 6 mm</td>
</tr>
<tr>
<td>Lobe Length</td>
<td>7.6 mm</td>
</tr>
<tr>
<td>Waist Length</td>
<td>9.0 mm</td>
</tr>
<tr>
<td>Sheath Diameter</td>
<td>12Fr</td>
</tr>
<tr>
<td>Stabilizing Wires</td>
<td>6 pairs</td>
</tr>
</tbody>
</table>

Temporal Trends Procedural Complications: ACP/Amulet

Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study

Methods and results: This multicentre prospective real-world registry included 1,088 patients (75±8.5 years, 64.5% male, CHA2DS2-VASc: 4.2±1.6, HAS-BLED: 3.2±1.1) with non-valvular atrial fibrillation; 82.8% of patients were considered to have an absolute or relative contraindication to long-term anticoagulation and 72.4% had had a previous major bleeding. Periprocedural results, clinical outcomes up to the first three months and the available TEE results from the first scheduled follow-up (one to three months post-implant) are reported. Successful device implantation was achieved in 99.0% of patients. During the procedure and index hospitalisation, major adverse events occurred in 3.2% of patients. Patients were discharged on a single antithrombotic agent (32.0%), dual antithrombotics (54.9%) or on oral anticoagulant (18.9%). TEE follow-up within 23 days post procedure in 673 patients showed adequate (<3 mm jet) occlusion of the appendage in 98.2% of patients and device thrombus in 10 patients (1.3%), as evaluated by core laboratory analysis.

Table 5. Antithrombotic therapy at discharge.

Medication type

| No antithrombotic therapy | 2.0% |
| Single APT | 16.0% |
| Clopidogrel or another antiplatelet | 7.0% |
| DAPT | 54.3% |
| OAC (alone or combined with APT) | 18.9% |

Number of patients with event(s) (%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Early (within &lt;7 days post procedure or before patient discharge, whichever is later)</th>
<th>Late (&gt;7 days post procedure, within 3 months of implant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite of ischemic stroke, systemic embolism and cardiovascular death</td>
<td>7 (0.6%) 95% CI [0.3%, 1.3%]</td>
<td>15 (1.4%) 95% CI [0.8%, 2.3%]</td>
</tr>
<tr>
<td>MAE</td>
<td>39 (3.6%)* 95% CI [2.6%, 4.9%]</td>
<td>N/A</td>
</tr>
<tr>
<td>Embolisation</td>
<td>1 (0.1%) 95% CI [0.002%, 0.5%]</td>
<td>1 (0.1%) 95% CI [0.002%, 0.5%]</td>
</tr>
<tr>
<td>All SAE</td>
<td>61 (5.6%)* 95% CI [4.3%, 7.1%]</td>
<td>26 (2.4%)* 95% CI [1.6%, 3.5%]</td>
</tr>
</tbody>
</table>

LAA Occlusion with the Amplatzer™ Amulet™ device: Primary results of the prospective global Amulet Observational Study

Subjects Consented (N=118)

Subjects Enrolled (Implant Attempted) (N=1088)

Implanted (N=1078)

Follow-up rate at 2-year visit: 94.2%

3.6%

Early SAEs (0-7 days)

Pericardial effusion or tamponade 1.5%
Major vascular complication 0.9%
Ischemic stroke 0.4%
Death 0.3%
Device embolization 0.2%

Late SAEs (related to procedure/device; >7 days)

Device-related thrombus (DRT) 1.8%
Major bleeding event 0.5%

• N=1088 Jun2015-Sep2016
• 82.8% OAC contraindicated
• Implant success 99.0%

Hildick-Smith et al, Presented EuroPCR2019

3.6%

6.7%/yr

68% reduction

2.2%/yr

CHA2DS2-VASc Predicted

Observed Rate

Annualized Rate (%)

68% reduction
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 CHADS2 or CHA2DS2-VASc scores and are 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.

**US Indication**

**International Indication:**

The WATCHMAN LAA Closure Technology is intended to prevent thrombus embolization from the left atrial appendage and reduce the risk of life-threatening bleeding events in patients with non-valvular atrial fibrillation who are eligible for anticoagulation therapy or who have a contraindication to anticoagulation therapy.
Current CE Mark Labeling

Old DFU

- Lifelong ASA
- DAPT for 6 Months
- No NOAC usage
- Specific Dosages
  - Distinction between “OAC eligible” and “OAC Contraindicated” patients

New DFU

- ASA for at least 12 months
- DAPT for at least 3 months
- NOAC use specified
- Dosage at physician’s discretion
  - Consideration of patient preference, risk of bleeding, and stroke risk

---

Current US Directions for Use require a combination of short-term warfarin and DAPT in the 6 months following the implant.

---

**Table 15** Atrial fibrillation patients who are not eligible ("contraindicated") for long-term oral anticoagulation and require prevention of stroke and embolism

<table>
<thead>
<tr>
<th>Clinical situation and therapeutic concept</th>
<th>Consensus statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF patients with CHA2DS2-VASc score ≥2 (is female) who have absolute contraindications for long-term OAC may be considered for LAO if a maximum period (2-4 weeks) of a single antithrombotic can be given</td>
<td></td>
</tr>
</tbody>
</table>

---

**Patients with an indication for stroke prevention due to atrial fibrillation**

- Elevated bleeding risk
  - Patients with 1. ASS-BLGR ≥3
    - Elevated bleeding risk outside ASS-BLGR Score, e.g., warfarin, thrombolytics
    - Need for prophylaxis or repetitive triple therapy, e.g., severe OSA and anemia
    - Recent failure (based on contraindication to NOAC)

- Patients with individual and specific risk constellation for stroke
  1. Inefficient OAC, “stroke on warfarin”
  2. Electrically isolated LAA post ablation (indication for LAA occlusion controversial)

- Patient unwilling or unable to take OAC
  - Advise NOAC

- Contraindication to oral anticoagulation
  - NOAC
  - LAA occlusion* (may require antiplatelet therapy)

---

**OAC (NOACs/Vit K-antagonists)**

*Note: In case of strict contraindication to antiplatelet therapy, patient may not be eligible for LAA occluder implantation but for percutaneous LAA occlusion or percutaneous LAA sealing.
Real-World Usage of Antithrombotic Post-LAAC

<table>
<thead>
<tr>
<th>Patients Eligible for Short-Term Full-Dose OAC Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Post-implant</td>
</tr>
<tr>
<td>45 days</td>
</tr>
<tr>
<td>3 months</td>
</tr>
<tr>
<td>6 months</td>
</tr>
<tr>
<td>≥ 12 months</td>
</tr>
<tr>
<td>NVDAC</td>
</tr>
<tr>
<td>Clopidogrel</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>B. Post-implant</td>
</tr>
<tr>
<td>3 months</td>
</tr>
<tr>
<td>6 months</td>
</tr>
<tr>
<td>≥ 12 months</td>
</tr>
<tr>
<td>NVDAC</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients Ineligible for Short-Term Full-Dose OAC Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. Post-implant</td>
</tr>
<tr>
<td>1 month</td>
</tr>
<tr>
<td>3 months</td>
</tr>
<tr>
<td>6 months</td>
</tr>
<tr>
<td>≥ 12 months</td>
</tr>
<tr>
<td>Clopidogrel</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>D. Post-implant</td>
</tr>
<tr>
<td>3 months</td>
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<tr>
<td>6 months</td>
</tr>
<tr>
<td>≥ 12 months</td>
</tr>
<tr>
<td>NVDAC low-dose</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>E. Post-implant</td>
</tr>
<tr>
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<tr>
<td>6 months</td>
</tr>
<tr>
<td>≥ 12 months</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
</tbody>
</table>
WATCHMAN Release Criteria: PASS

All criteria must be met prior to device release (PASS)

**Position** – device is distal to or at the ostium of the LAA

**Anchor** – fixation anchors engaged / device is stable

**Size** – device is compressed 8-20% of original size

**Seal** – device spans ostium, all lobes of LAA are covered
WATCHMAN: Compression & Seal

• Device compression 8-20%
• Peri-device leak <5mm

Suggested Algorithm for Device Surveillance

Endovascular LAAC

1st TEE 6-12wks post-LAAC*

Peri-device leak >5mm

Continue OAC/NOAC/DAPT

Repeat TEE 6-12wks

2nd TEE 12mths post-LAAC*

Device-related thrombosis (DRT)

Treatment (table 3)

Repeat TEE 8-12wks

DRT still present

DRT resolved

Intensify treatment (consider):
1. Warfarin INR 2.5-3.5 ± aspirin
2. LMWH ± aspirin
3. Surgical excision

Repeat TEE 3-6mth

*CTA can be alternative if TEE cannot be done

Future Directions for LAA Closure

- New LAAC devices
- New randomized controlled trials (contra-indicated population, vs. DOAC, etc)
- Combined procedures with LAAC
- Peri-procedural Imaging with LAAC
- Minimalist approach with LAAC

Single Lobe Design
- Watchman™ FLX
- Occlutech
- Conformal
- WaveCrest
- Prolipsis

Lobe & Disc Design
- Amulet
- Ultraceal
- LAmbre
- SeaLA
### Clinical Studies for New Endovascular Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>CE Mark</th>
<th>Major Trials Ongoing/Planned</th>
</tr>
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<tbody>
<tr>
<td>Watchman FLX</td>
<td>Boston Scientific</td>
<td>2015</td>
<td>EU &amp; US prospective registry (PINNACLE FLX, n=400) completed. Non-inferiority comparison to WM2.5</td>
</tr>
<tr>
<td>Amulet</td>
<td>Abbott Vascular</td>
<td>2013</td>
<td>Amulet-PMR (n=1088): Completed 2yr FU Amulet IDE study (RCT vs WM): completed 1800pt global</td>
</tr>
<tr>
<td>WaveCrest</td>
<td>Coherex</td>
<td>2013</td>
<td>WAVECREST-II: IDE (RCT vs WM), 1250pt, started early 2018</td>
</tr>
<tr>
<td>Lambre</td>
<td>Lifetech</td>
<td>2016</td>
<td>Planned REDUCE-1 (RCT vs WM, n=1800), REDUCE-2 (Lambre vs antiplatelet for OAC contraindicated, n=800)</td>
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<td>Oclutech</td>
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<td>2016</td>
<td>Ongoing phase 2 study (n=105)</td>
</tr>
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<td>Ultrasel</td>
<td>Cardia</td>
<td>2017</td>
<td>Ongoing phase 2 (&gt;600 implanted)</td>
</tr>
<tr>
<td>SeaLA</td>
<td>NA</td>
<td>NA</td>
<td>FIM 11pt implanted. Planned 226pt multi-country registry</td>
</tr>
<tr>
<td>Prolipsis</td>
<td>Custom Medical</td>
<td>NA</td>
<td>Planned FIM clinical trial</td>
</tr>
<tr>
<td>Conformal</td>
<td>Conformal Medical</td>
<td>NA</td>
<td>Ongoing FIM trial (n=15)</td>
</tr>
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### WATCHMAN FLX: Design Features

- **10 Strut Frame**
  - Partial Recapture
  - Minimum LAA Depth = Ostium Dia.
  - One row of 10 Anchors
- **18 Strut Frame**
  - Full or Partial Recapture
  - Minimum LAA Depth = ½ Device Size
  - Two rows of 18 Anchors

**Increased Sizing Range**

<table>
<thead>
<tr>
<th>8 - 20% Compression</th>
<th>10 - 30% Compression</th>
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</thead>
<tbody>
<tr>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>24</td>
<td>27</td>
</tr>
<tr>
<td>31</td>
<td>35</td>
</tr>
</tbody>
</table>

**Ostium Diameter (mm)**

- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
PINNACLE FLX IDE Study

A US-only IDE to evaluate the safety and efficacy of the new WATCHMAN FLX Device

**Study Design**
- Single arm non-randomized study design
  - DOAC only options for post-implant drug regimen
  - Non-inferiority to performance goal based on current generation WATCHMAN

**Enrollment**
- 400 Patients at 29 U.S sites

**Primary Endpoints**
- **Safety Endpoint**
  - The occurrence of one of the following events between the time of implant and within 7 days following the procedure or by hospital discharge, whichever is later: all-cause death, ischemic stroke, systemic embolism, or device- or procedure-related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair.

- **Efficacy Endpoint**
  - The rate of effective LAA closure defined as any peri-device flow < 5mm demonstrated by TEE at 12 months

**Secondary Endpoints**
- The occurrence of ischemic stroke or systemic embolism at 24 months from the time of enrollment

**Follow-Up**
- 45 days, 6 months, 12 months, 18 months, and 24 months

**Status**
- Enrollment Complete

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### Clinical Studies for Epicardial Devices

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</tr>
</thead>
<tbody>
<tr>
<td>Lariat</td>
<td>SentreHeart</td>
<td>2015</td>
<td>AMAZE study ongoing (n=600): LARIAT+PVI vs PVI alone (Freedom from AF&gt;30s at 12mth post-PVI)</td>
</tr>
<tr>
<td>Sierra Ligation</td>
<td>Aegis</td>
<td>NA</td>
<td>Ongoing early feasibility study in Canada and US (LASSO-AF, n=30)</td>
</tr>
<tr>
<td>Atriclip</td>
<td>Atricure</td>
<td>2016</td>
<td>• &gt;120,000 devices implanted to-date (can be thoracoscopic)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• EXCLUDE: n=70 non-RCT cardiac surgery, 69/70 TEE excluded LAA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ATLAS: RCT 2:1, Atriclip vs control (pt w/o documented AF but with CHADS-VASc&gt;3 and HASBLED&gt;3 and undergoing valve or CABG with direct visual access to the LAA). Up to 2000pts.</td>
</tr>
</tbody>
</table>

### Major Ongoing/Planned LAA Closure RCT

<table>
<thead>
<tr>
<th>Study</th>
<th>RCT Comparisons</th>
<th>N</th>
<th>Study Population &amp; Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAP-TOO</td>
<td>2:1 Watchman vs single/no antiplatelet tx</td>
<td>888</td>
<td>OAC contraindicated pts. 1° endpoint: time to 1st ischemic stroke &amp; systemic embolization. 100 global sites.</td>
</tr>
<tr>
<td>STROKE-CLOSE</td>
<td>2:1 Amulet vs control (OAC, antiplatelet, or none)</td>
<td>750</td>
<td>Prior intracerebral hemorrhage pts. 1° endpoint: stroke, SE, life-threatening or major bleed, and all-cause mortality.</td>
</tr>
<tr>
<td>PRAGUE-17</td>
<td>1:1 Watchman or Amulet vs DOAC</td>
<td>396</td>
<td>1° endpoint: stroke, systemic CV event, clinically significant bleed, CV death, or procedure/device-related complications</td>
</tr>
<tr>
<td>CLOSURE-AF</td>
<td>1:1 LAAC vs med tx</td>
<td>1400</td>
<td>OAC contraindicated (HASBLED&gt;2, prior bleed, GFR&lt;30). 1° endpoint: stroke, SE, CV/unexplained death, major bleed</td>
</tr>
<tr>
<td>REDUCE-2</td>
<td>1:1 LAmbr vs antiplatelet</td>
<td>800</td>
<td>OAC contraindicated pts. *Unclear status.</td>
</tr>
</tbody>
</table>
### Study Objective
Evaluate LA Closure with WATCHMAN in NVAF patients deemed **not suitable for oral anticoagulation** therapy.

### Study Design
Prospective, multi-center
Randomized 2:1 (Watchman vs. Control)
Group Sequential Design, Superiority trial, intention-to-treat

### Primary Endpoint
**Effectiveness Endpoint**
Time to first occurrence of ischemic stroke or systemic embolism

**Safety Endpoint**
7-day rate of all-cause death, ischemic stroke, systemic embolism, or device- or procedure-related events requiring open cardiac surgery or major endovascular intervention

### Patient Population
888

### Number of Sites
120 global sites (>65 US, >35 international)

### Follow-up
- 3 month with TEE
- 12 month with TEE
- 6, 18 month phone visit
- Bi-annually for years 2-5

### Study Funding
Boston Scientific. PI: V. Reddy, J. Saw, M. Buchbinder

---

### ASAP-TOO Study: Update Aug2019

**Randomized Subjects**

<table>
<thead>
<tr>
<th>Total Randomization Goal</th>
<th>888</th>
</tr>
</thead>
<tbody>
<tr>
<td>200</td>
<td></td>
</tr>
<tr>
<td>400</td>
<td></td>
</tr>
<tr>
<td>600</td>
<td></td>
</tr>
<tr>
<td>800</td>
<td></td>
</tr>
</tbody>
</table>

**Authorized Sites**

<table>
<thead>
<tr>
<th>Total Site Goal</th>
<th>Up to 120</th>
</tr>
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<tbody>
<tr>
<td>20</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td></td>
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<tr>
<td>60</td>
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<tr>
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<tr>
<td>100</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td></td>
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</tbody>
</table>

**Average Randomization Rate = 0.20 Subjects/Site/Month**

- The GOAL is for each site to have a randomization rate ≥ 0.5 subjects per month
- 10% (10/98) of sites are meeting this goal
**Major Ongoing/Planned LAA Closure RCT**

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**Percutaneous left atrial appendage closure versus novel anticoagulation agents in high-risk atrial fibrillation patients (PRAGUE-17 study)**

Primary Endpoint: a composite of:
1. Stroke or transient ischemic attack (TIA)
2. Systemic embolism
3. Clinically-significant bleeding *
4. Cardiovascular death, or
5. Significant peri-procedural or device-related complication.

• Apixaban - 192 patients (95.5%):
  - 2 x 5 mg in 33 (16.4%) patients
  - 2 x 2.5 mg in 33 (16.4%) patients
• Dabigatran - 8 patients
  - 2 x 150 mg in 7 (3.5%) patients
  - 2 x 110 mg in 1 (0.5%) patient
• Rivaroxaban - 1 patient (0.5%)
  - 1 x 20 mg daily

---

Cumulative incidence function (CIF) for primary study endpoint in intention-to-treat populations

Gray’s test; p = 0.44
Subdistribution HR: 0.84 (0.53 – 1.31), p = 0.44
Non-inferiority: p = 0.004

Osmancik P, et al. Presented at ESC.
### Combined Procedures With LAAC: TAVR

<table>
<thead>
<tr>
<th>Study</th>
<th>Devices</th>
<th>N</th>
<th>Study Population &amp; Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>WATCH-TAVR</td>
<td>TAVR + Watchman (n=156 combined) vs TAVR alone (n=156)</td>
<td>312</td>
<td>RCT (up to 400pt). 1st occurrence of all-cause mortality, stroke (ischemic or hemorrhagic), or bleeding (life-threatening and major) events through 1 y</td>
</tr>
<tr>
<td>TAVI-LAAO</td>
<td>TAVR + Amulet (LAAC during TAVR or index hosp)</td>
<td>80</td>
<td>RCT (3 Switzerland centers) vs. TAVR alone: Severe AS + AF (CHADS-VASC ≥1)</td>
</tr>
<tr>
<td>TAVI-LAAC</td>
<td>Simultaneous Watchman + Accurate</td>
<td>50</td>
<td>Prospective registry. 1st endpoint (30d safety): mortality, stroke, life-threatening bleed, acute kidney injury, coronary artery obstruction requiring intervention, major vascular complications, valve-related dysfunction requiring repeat procedure, pericardial effusion requiring drainage, device embolization requiring surgical intervention</td>
</tr>
</tbody>
</table>

### Combined Procedures With LAAC: AF Ablation

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>N</th>
<th>Study Population &amp; Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phillips et al</td>
<td>2017</td>
<td>139</td>
<td>Pooled EWOLUTION &amp; WASP. 10 centers. Successful LAAC 100%. Pericardial effusion 1.4%, tamponade requiring intervention 0.7%, no periprocedural stroke/death. 30-day SAE 8.7%. No stroke, device embolization, or death at 30 days. 30-day bleeding SAE 2.9% (55% NOAC and 38% warfarin post-procedure). Peridevice leaks increased significantly from 2.9% at implant to 39% at first follow-up.</td>
</tr>
<tr>
<td>Pelissero et al</td>
<td>2017</td>
<td>21</td>
<td>21 LAAC+ablation, 21 controls with OAC. 100% LAAC success. Longer procedural time with combined (68 vs 52min), and 1 AV fistula</td>
</tr>
<tr>
<td>Hu et al</td>
<td>2017</td>
<td>34</td>
<td>100% successful ablation + LAAC, no leak, no DAT or peri-device leak at FU 3mth. No complication.</td>
</tr>
<tr>
<td>Phillips et al</td>
<td>2016</td>
<td>98</td>
<td>Successful LAAC 94%. Complete LAA occlusion rate 84%. 1 stroke at mean 802d FU. 12mth AF freedom 77%.</td>
</tr>
<tr>
<td>Fassini et al</td>
<td>2016</td>
<td>35</td>
<td>86% complete sealing; 5 patients had residual flow (&lt;5 mm) at first TEE, but only 3 at 1-yr TEE</td>
</tr>
<tr>
<td>Calvo et al</td>
<td>2015</td>
<td>35</td>
<td>Successful ablation + LAAC 97%. 3 cardiac tamponade. 100% seal at 3mths. Mean FU 13mths, 78% were free of arrhythmia recurrences and OAC withheld in 97%.</td>
</tr>
</tbody>
</table>
**OPTION Trial:** To determine if left atrial appendage closure with the WATCHMAN Device is a reasonable alternative to oral anticoagulation following catheter ablation for patients with NVAF.

Approximately 1600 subjects at 130 sites world-wide
Randomized 1:1 (Device to OAC)
Follow-Up at 3, 12, 24, and 36 months

**Patient Populations**

- **Sequential**
  - Prior ablation procedure for NVAF between 3 and 6 months prior to randomization

OR

- **Concomitant**
  - Planning to have catheter ablation within 10 days of randomization

**Medication Regimens**

- **Device Group**
  - Market approved OAC and aspirin (75-100mg recommended) for 90 days followed by aspirin through at least 12-months post-implant (recommended for duration of the trial).

- **Control (OAC) Group**
  - Market approved OAC used per IFU for atrial fibrillation stroke preventions for the duration of the trial.

*Note: This trial will be run using investigational product (WATCHMAN FLX)  *BSC is not reimbursing for concomitant procedures

**LAAC Peri-Procedural Imaging**
CCTA Can Guide Watchman Sheath Selection

3D Printing

Validation of a computational model aiming to optimize preprocedural planning in percutaneous left atrial appendage closure

Alessandra M. Bevo1,2, Benjamin T. Wilkins3, Philippe Garot4, Sander De Bock5, Jacqueline Saw6, Lars Søndergaard2, Ole De Backer2, Francesco Innamorato2

• CCT-based computational model (FEops HEARTguide™)
• 30pt LAAC (Amulet=15, Watchman=15) and having pre- and post-procedural CCT-scan were selected
• Coefficient of determination (R²) between model and actual device was ≥0.91
• Difference in measurements between model and actual device (area, perimeter, minimum diameter, maximum diameter) was ≤5%

Comparison of cardiac computed tomography angiography and transoesophageal echocardiography for device surveillance after left atrial appendage closure

Sadia R. Qamar1, MBBS; Sabeena Jalal2, MBBS, MSc; Savvy Nichols3, MD; Michael Tsung4, MD, Thomas Gilbert5, MD, Jacqueline Sauf6, MD

• N=102, CCTA & TEE post-LAAC
• 79 Watchman, 23 ACP/Amulet
• CCTA mean 105.2±54.8d, TEE 124.9±100.3d
• PDL 34.3% TEE, contrast patency 51.0% CCTA (p=0.016) (86.5% PDL, 13.5% fabric-leak)
• Moderate correlation between the leak size on CCTA versus TEE (r=0.484, p=0.007)
• Device compression greater with sealed devices (11.3% vs. 8.2%, p<0.001)
• 1 DRT (seen on both CCTA & TEE)
• No adverse clinical events with residual PDL
LAAC: Minimalist Approach?

**Intracardiac Echocardiography for Endovascular Left Atrial Appendage Closure**  
*Is It Ready for Primetime?*

**TABLE 1** Observational series of ICE-guided LAA closure  

<table>
<thead>
<tr>
<th>First Author (Ref.)</th>
<th>Year</th>
<th>N</th>
<th>ICE Position</th>
<th>LAA Device</th>
<th>Technical Success</th>
<th>Procedural Success</th>
<th>Study Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mraz et al. (2)</td>
<td>2007</td>
<td>30</td>
<td>RA</td>
<td>PLAATO</td>
<td>100%</td>
<td>NA</td>
<td>Procedural TEE in all patients. ICE only to guide transseptal puncture and positioning of the guide catheter.</td>
</tr>
<tr>
<td>Berti et al. (3)</td>
<td>2014</td>
<td>121</td>
<td>RA, CS</td>
<td>ACP Amulet</td>
<td>96.7%</td>
<td>93.4%</td>
<td>Pre-procedural TEE. Procedural ICE &amp; fluoroscopy. No follow-up TEE reported.</td>
</tr>
<tr>
<td>Masson et al. (4)</td>
<td>2015</td>
<td>37</td>
<td>LA (double transseptai)</td>
<td>ACP</td>
<td>97.3%</td>
<td>89.2%</td>
<td>Pre-procedural TEE. Procedural ICE &amp; fluoroscopy. TEE at 3 months, only 3.3% leak.</td>
</tr>
<tr>
<td>Matsuo et al. (5)</td>
<td>2016</td>
<td>27</td>
<td>RA (or LA or LLVP)</td>
<td>Watchman</td>
<td>100%</td>
<td>96.3%</td>
<td>Pre-procedural TEE. Procedural ICE &amp; fluoroscopy. TEE at 45 days, no flow 51.9%, &lt;5-mm flow 48.7%.</td>
</tr>
<tr>
<td>Frangieh et al. (6)</td>
<td>2016</td>
<td>32</td>
<td>LA (single transseptai)</td>
<td>Watchman</td>
<td>100%</td>
<td>100%</td>
<td>Pre-procedural TEE. Procedural ICE &amp; fluoroscopy. When compared to 44 TEE-guided cases, longer time to transseptal puncture and closure with ICE.</td>
</tr>
<tr>
<td>Kondsholm et al. (7)</td>
<td>2017</td>
<td>109</td>
<td>LA (single transseptai)</td>
<td>ACP Amulet</td>
<td>99.1%</td>
<td>94.5%</td>
<td>Pre-procedural CTA. Procedural ICE &amp; fluoroscopy. No difference in success and complication rates compared to TEE.</td>
</tr>
</tbody>
</table>
Other approaches?
- Fluoroscopy alone?
- Micro-TEE

Methods: A comprehensive literature search was performed in PubMed, Embase, Scopus, Google Scholar, and major scientific conference sessions for published abstracts and manuscripts until 31 August 2018. Studies reporting clinical outcomes comparing TEE vs ICE for endocardial LAAC in human subjects aged greater than or equal to 18 years were included. Two investigators independently extracted the data and individual quality assessment was performed. The analysis was performed using Cochrane Collaboration software, RevMan 5.3.

Results: Five eligible studies consisting of 1157 patients (ICE:391 patients and TEE:766 patients) were included. Four studies were retrospective and one was prospective, nonrandomized. Two studies included Watchman, two included the Amplatzer Cardiac Plug/Amulet device, and one included both devices. There was no significant difference in CHA2DS2-VASC or HAS-BLED scores between both groups. There was no significant difference in acute procedural success between ICE vs TEE (risk ratio, 1.01; 95% CI, 0.99-1.03; P = 0.24). There was no significant difference in fluoroscopy time (mean difference [MD], 1.84 minutes; 95% CI, 0.59-2.75; P = 0.14) and total procedure time (MD, 5.06 minutes; 95% CI, 2.64-14.4; P = 0.61) between both groups. There was also no significant difference in complications including pericardial tamponade, device embolization, and stroke between both groups. Conclusion: In our meta-analysis, ICE was as effective as TEE during percutaneous LAAC.
Feasibility, Safety, and Utility of Microtransesophageal Echocardiography Guidance for Percutaneous LAAO Under Conscious Sedation

50 LAAO (28 Amulet, 17 WM, 6 Lambre)
- Micro-TEE: 5 transnasal (2 mild epistaxis), remainder transoral
- Local anesthesia (IV midaz, fentanyl)
- Good airway tolerance, no need for regular TEE
- Image quality good 73.5% or acceptable 26.5%
- Successful LAAO all cases, no complication, 1 needed 2nd device
- FU 45d TEE: PDL >3mm in 8%, no DRT
- Reduced procedural time (78 vs 53min, p<0.05)

We present our experience with a miniaturized TEE probe (micro-TEE) (88-35, Koninklijke Philips N.V., Amsterdam, the Netherlands) for LAAO guidance. It is a sectorial probe, 3 to 8 MHz plane rotation 0° to 180°, anteposterior deflectable distal end, 3-dimensional imaging, color and pulsed or continuous Doppler, length 8.5 cm, diameter 5.2 mm, and distal length 7.5 × 5.5 mm. It provides neither tridimensional nor 2-dimensional orthogonal imaging.

Yoga Yuniadi MD, PhD  |  Dicky A. Hanafy MD  |  Sunu B. Raharjo MD, PhD  |  Dony Yugo MD

CHARACTERISTICS
- Fluoroscopic guided (Group A)
- TEE guided (Group B)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Fluoroscopic guided (Group A)</th>
<th>TEE guided (Group B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>66.16 ± 8.79</td>
<td>67.42 ± 9.8</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Persistent</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Long-standing persistent</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Permanent</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
<td>4.29 ± 1.51</td>
<td>3.54 ± 1.67</td>
</tr>
<tr>
<td>HASBLED score</td>
<td>3.13 ± 0.99</td>
<td>2.64 ± 1.06</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>64 ± 10.5</td>
<td>61 ± 16</td>
</tr>
<tr>
<td>Left atrial dimension (mm)</td>
<td>48 ± 9.67</td>
<td>42.9 ± 7.82</td>
</tr>
</tbody>
</table>

Results: Twenty-five subjects were implanted ACP by means fluoroscopy only (Group A) and 28 subjects using standard technique group (Group B). The median AF duration was 36 months (6-276 months) and majority of patients (49%) are having permanent AF. The mean CHA2DS2-VASc score is 3.9 ± 1.53. Successful implantation of ACPs was 96% in both groups. Nonfatal periocardial effusion occurred in three patients. During 75 weeks of follow-up period, there were no significant differences of stroke event and death between groups.

Conclusion: ACP implantation guided with fluoroscopy only is feasible and safe.
Safety and Feasibility of Same-Day Discharge after Left Atrial Appendage Closure

Thomas Gilhofer, Taku Inohara, Ashkin Parsa, Minette Walker, Naomi Uchida, Michael Tsang, Jacqueline Saw
The University of British Columbia, Department of Medicine, Vancouver General Hospital

Background: Percutaneous left atrial appendage closure (LAAC) is increasingly performed as an alternative to oral anticoagulation (OAC) for atrial fibrillation stroke prevention. The success and complication rates with LAAC have dramatically improved with maturing experience, growing procedural familiarity, and pre-procedural planning. This has enabled same-day discharge (SDC) post-LAAC and we report the first series.

Methods: We included all patients who were discharged same-day post-LAAC at Vancouver General Hospital. Informed consents were obtained for prospective follow-up in LAAC registry. LAAC indications were CHADS-VASc≥2 and unsuitability for OAC. Pre-procedural selection for SDC was based on physician and image coordinator clinical judgement on patients’ overall physical condition, lack of significant frailty (Canadian Study of Health and Aging clinical frailty scale ≥3) or co-morbidities, good home support, and patient preference. Selected patients were scheduled in the morning and continued SDC pathway if LAAC was successful without complication. Prograde pre-procedure was performed for all femoral venous punctures. LAAC was guided with transesophageal echocardiography (TEE) under general anesthesia, or intracardiac echocardiography (ICE) under local anesthesia. Pre-discharge transesophageal echocardiography was performed to rule-out device embolization and peri-procedural effusion, and repeated next day as-out-patient.

Results: Twenty-two patients were discharged same-day after WATCHMAN (n=11) or Amulet (n=11) LAAC from 1/6/2018-3/31/2018. Mean age was 76.6±7.7 yrs (range 57-91), CHADS-VASc 4.1±1.4, HAS-BLED 3.7±1.0. Nineteen were TEE-guided, 3 were ICE-guided. Procedural success was 100% with no complication. Mean procedural time was 66.4±16.9min and fluoroscopy time 13.6±9.2min. Patients were discharged at mean 202±55.8min after having procedural room, and all were discharged on aspirin and clopidogrel post-LAAC. There was 1 femur tear, but no other procedure-related complication within 1-month follow-up.

Conclusion: SDC is safe in carefully selected patients post-LAAC with dedicated pathway and surveillance. This may have tremendous implications on healthcare cost-savings.

LAA Closure: Summary

- Clear clinical need for LAAC, especially for patients not suited for OAC
- LAAC can be performed safely, with good technical success, and with effective long-term results
- Routine device surveillance important to assess for device-related issues (DRT, peri-device leak, migration/embolization)
- Ongoing important RCT to assess: contraindicated populations, device vs. device, device vs. DOAC, combination with TAVR/ablation
- Novel approaches to peri-procedural imaging & guidance (non-GA TEE), & minimalist approach, are gaining traction