Joint Symposium with Neurology
Non-Pharmacologic Stroke Prevention

Seung Yong Shin, M.D., PhD.
Cardiovascular & Arrhythmia Center
Chung-Ang University, Seoul, Republic of Korea
Conflicts of Interest

Nothing to disclose
NOAC has Markedly Changed our SPAF

• AF epidemic: 33 million AF patients in the world


• About 230,000 Korean AF patients with CHA$_2$DS$_2$-VASc $\geq$ 2, requires oral anticoagulation in 2015

  Lee SR, Choi EK et al. Int J Cardiol 2017;236:226-231

• Approximately 83 % of AF patients use NOACs

  Kim HS, Joung BY et al. Korean Circ J 2017; 47(6): 877-87

• In pooled comparison with warfarin, NOAC decreased hemorrhagic stroke by 51 % ($P < 0.0001$)

  Ruff CT et al. Lancet 2014; 383; 955-62

• In recent meta-analysis, major GI bleeding was similar between NOACs and VKA

Why Non-pharmacologic SPAF?

• Major GI bleeding is not uncommon problem in elderly patients requiring anticoagulation (1~1.5%)

• In elderly patients, their bleeding risks are not modifiable (elderly, advanced chronic kidney disease, multiple comorbidities, drug interaction...)

• With systemic anticoagulation strategies, we cannot maintain a balance between bleeding and thrombosis

Why LAA?

Most thrombi (90%) in NVAF develop in LAA

Courtesy of Prof. J Hong
220 Post-mortem analysis (106 male, 114 female)
Age: 72 ± 13 years
Rhythm: Sinus rhythm 143, AF 55
Volume: 770~19,270 mm$^3$ (5,220 ± 3,041 mm$^3$)
Angulation: > 100° (42%)
Narrow diameter: 5~27 mm
Wide diameter: 10~40 mm
Length: 16~51 mm
AF vs. Sinus rhythm: 7060 mm$^3$ vs. 4645 mm$^3$ (P < 0.01)
Development of LAA

5 Weeks

- Primordial left atrium

8 Weeks

- Left auricle

Hara et al. CCI.2009;74:234-242
Various Shapes of LAA

cactus  cauliflower  chicken wing  windsock
Benefits of LAA Exclusion

- In the surgical closure era...
  - LAA has been proposed TE source since 1940’s
    Madden JL, JAMA 1948;140:769-
  - 50% of thrombi in LAA, in patients with MV disease
    Jordan RA et al. Circulation 1950; 3:363-
  - 64% of patients with mitral surgery experience TE
    Belcher JR et al. BMJ 1955;2:1000-
  - In the 1990’s, Cox proposed LAA amputation as an integral part of surgical procedure
    Cox JL et al. JTCVS 1991;101:584-
From 7 Surgical Studies...

<table>
<thead>
<tr>
<th>Author</th>
<th>Period</th>
<th>Type of study</th>
<th>Number of LAA</th>
<th>Number of non-LAA</th>
<th>LAA occlusion method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al.</td>
<td>1999-2011</td>
<td>Propensity-score matched</td>
<td>119</td>
<td>119</td>
<td>LAA amputation during crio-Maze</td>
</tr>
<tr>
<td>Whitlock et al.</td>
<td>2009-2010</td>
<td>Miscellaneous</td>
<td>26</td>
<td>25</td>
<td>Amputation and stapler</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2001-2010</td>
<td>Propensity-score matched</td>
<td>631</td>
<td>631</td>
<td>Amputation or closure of LAA</td>
</tr>
<tr>
<td>Zapolanski et al.</td>
<td>2005-2012</td>
<td>Observational</td>
<td>808</td>
<td>969</td>
<td>Double ligature with suture</td>
</tr>
<tr>
<td>Nagpal et al.</td>
<td>2007</td>
<td>RCT</td>
<td>22</td>
<td>21</td>
<td>Amputation, suture</td>
</tr>
<tr>
<td>Healey et al.</td>
<td>2001-2002</td>
<td>RCT</td>
<td>52</td>
<td>25</td>
<td>Suture or stapler</td>
</tr>
<tr>
<td>Garcia-Fernandez et al.</td>
<td>1996-2001</td>
<td>Observational</td>
<td>58</td>
<td>147</td>
<td>Ligature of LAA with endocardial suture</td>
</tr>
</tbody>
</table>

LAA, left atrial appendage; RCT, randomized controlled trial.

Total 3,653 patients (1716 – LAAO, 1937 – Non-LAAO)
Mainly MV surgery, Aorto-coronary surgery mixed
Surgical suture in 4 study, Amputation in 2 study, Mixed in 1 study

RESULTS

**Stroke incidence** reduced in LAAO
**Mortality** reduced in LAAO
Bleeding requires reoperation – not different

Casu et al. Eur Heart J 2017:19S;D333-
# Landmark Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Devices</th>
<th>Population</th>
<th>Primary efficacy endpoints</th>
<th>Other endpoints</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLAATO2</td>
<td>Prospective multicenter non-randomized study</td>
<td>PLAATO device (N = 180)</td>
<td>180</td>
<td>Successful LAOO determined by TEE at 2M F/U. Device performance endpoints defined as technical and procedural success.</td>
<td>MAE from hospitalization to 24M after IP.</td>
<td>PEE: 126/140 patients with TEEs had LAOO (90%, 95%CI 83.5% to 94.2%) PSE: 16 MAE in 129 PY (12.4%, 95%CI 7.5% to 19.6%)</td>
</tr>
<tr>
<td>Protect AF Trial3</td>
<td>Randomized control trial</td>
<td>Watchman (n = 463) versus warfarin (n = 244)</td>
<td>707</td>
<td>Composite primary endpoint of non-inferiority to warfarin</td>
<td>Safety events related to excessive bleeding or procedure-related complications</td>
<td>PEE: 3.0 (IG) vs 4.9 (CG) per 100 PY PSE: 7.4 (IG) vs 4.4 (CG) per 100 PY 99.9% probability of noninferiority</td>
</tr>
<tr>
<td>Prevail Trial4</td>
<td>Multicenter randomized control trial</td>
<td>Watchman (n = 269) versus warfarin (n = 138)</td>
<td>407</td>
<td>PEE: stroke, systemic embolism, cardiovascular/unexplained death in LAOO vs warfarin; overall and after 7 days (late ischemic PEE)</td>
<td>Safety endpoint of All-cause death, stroke, SE, or device-/procedure-related events within 7 days</td>
<td>PEE: 0.064 (IG) vs 0.063 (CG) with 18M rate ratio 1.07 (did not meet non-inferiority criteria). Late-Ischemic PEE: 0.0253 (IG) vs 0.0200 (CG) met non-inferiority criteria after 7 days PSE: 2.2% of subjects had an event, safety endpoint was achieved.</td>
</tr>
<tr>
<td>ASAP Study7</td>
<td>Multicenter, prospective, nonrandomized study</td>
<td>Watchman (n = 150)</td>
<td>150</td>
<td>PEE: combined events of stroke, SE, and CV/unexplained death</td>
<td></td>
<td>Observed ischemic stroke 1.7% per year, represents 77% fewer events than expected</td>
</tr>
<tr>
<td>CAP Registry5</td>
<td>PROTECT AF registry</td>
<td>Watchman (n = 460)</td>
<td>460</td>
<td>Safety events</td>
<td></td>
<td>Procedure or device-related safety endpoint 3.7%, a relative reduction of 56% from protect AF trial</td>
</tr>
</tbody>
</table>

AE, adverse events; CI, confidence interval; CG, control group; CV, cardiovascular; IG, intervention group; IP, index procedure; M, months; MAE, major adverse events; PEE, primary efficacy endpoint; PSE, primary safety endpoint; SE, systemic embolus
Pooled Meta-analysis

(A) Overall mortality

- LAAC vs Placebo: HR 0.38 (0.22–0.67)
- LAAC vs APT: HR 0.58 (0.37–0.91)
- LAAC vs NOAC: HR 0.76 (0.50–1.16)

(B) Stroke or systemic embolism

- LAAC vs Placebo: HR 0.24 (0.11–0.52)
- LAAC vs APT: HR 0.44 (0.23–0.86)
- LAAC vs NOAC: HR 1.01 (0.53–1.92)
Pooled Meta-analysis

(A) Major bleeding

LAAC vs Placebo

\[ HR = 2.33 \ (0.67-8.09) \]

LAAC vs APT

\[ HR = 0.75 \ (0.30-1.88) \]

LAAC vs NOAC

\[ HR = 0.80 \ (0.33-1.94) \]
Pooled Meta-analysis

(B)

Intracranial bleeding

LAAC vs Placebo
HR (95% CI) = 0.36 (0.04–3.31)

LAAC vs APT
HR (95% CI) = 0.42 (0.11–1.61)

LAAC vs NOAC
HR (95% CI) = 0.44 (0.13–1.49)
Pooled Meta-analysis

(C) Gastrointestinal bleeding

LAAC vs Placebo: HR (95% CI) = 1.81 (0.24–13.41)

LAAC vs APT: HR (95% CI) = 0.42 (0.10–1.87)

LAAC vs NOAC: HR (95% CI) = 0.22 (0.09–0.56)
LAAO in Major GI Bleeding

- From ACP Multicenter Registry
- 151 patients with major GI bleeding (MGIB), 1.3 Yr
- More frequent peri-procedural bleeding
  
  4.0 % vs. 0.8 %, P = 0.001

- Stroke / TIA 2.1 % (61.4% risk reduction, C-V score)
- MGIB 4.6% (20.1% risk reduction, HASBLED score)

Lempereur M et al. Am J Cardiol. 2017;120:414-
Several Limitations

- High failure rate (50% - incomplete occlusion)  
Katz ES et al. JACC 2000;36:468-

- Thrombi in LAA – 25% by TEE  
Kanderian AS et al. JACC 2008;52:924

- Surgical removal of LAA – Risk of tearing, extremely fragile structure, difficulties in hemostasis, not widely used  
Healey JS et al. Am Hearg J 2005;150:288-

In spite of several limitations, LAAO is effective in stroke reduction
Endothelialization After LAA Occlusion -PLAATO Device, Canine Model-

Endothelialization After WATCHMAN In Canine Model

Implanted device

45 days

Complete endothelialization
Procedural Complexity
Major Complication Rates

Mainly due to anatomical complexity of LAA
→ Comprehensive anatomical assessment & assistance

### Procedural Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Aggregate Clinical Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Procedures</td>
<td>6,720</td>
</tr>
<tr>
<td>Implantation Success, %</td>
<td>94.9%</td>
</tr>
</tbody>
</table>

### Complication Rates

<table>
<thead>
<tr>
<th>Complication Type</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial Tamponade</td>
<td>1.24%</td>
</tr>
<tr>
<td>Procedure-Related Stroke</td>
<td>0.18%</td>
</tr>
<tr>
<td>Device Embolization</td>
<td>0.25%</td>
</tr>
<tr>
<td>Procedure-Related Death</td>
<td>0.06%</td>
</tr>
</tbody>
</table>
Remaining Issues

• How can we improve procedural safety?
  ➔ Intra-procedural safety and outcome can be improved with intra-cardiac echocardiography (ICE)

  ➔ Pre-procedural planning with 3D printed model can improve procedural safety and outcome

• LAAO can accelerate diastolic dysfunction in patients with less remodeled LA

• Who can stop anticoagulation after LAAO?
  ➔ Needs to be addressed... and more...


Cho IS... Shin SY et al. ESC 2019 poster presentation

Phan QT... Shin SY et al. Cardiol J. May 2. doi: 10.5603/CJ.a2018.0047
With ICE (Intra-cardiac Echocardiography)

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Subjects (n = 135)</th>
<th>ICE group (n = 32)</th>
<th>No ICE group (n = 103)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72.2 ± 9.4</td>
<td>71.9 ± 10.4</td>
<td>72.3 ± 9.2</td>
<td>0.813</td>
</tr>
<tr>
<td>Male</td>
<td>72 (53.3 %)</td>
<td>21 (65.5 %)</td>
<td>51 (49.5 %)</td>
<td>0.155</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>39 (28.9%)</td>
<td>11 (34.4 %)</td>
<td>28 (27.2 %)</td>
<td>0.504</td>
</tr>
<tr>
<td>CHA₂DS₂-VASc score</td>
<td>4.3 ± 1.4</td>
<td>4.3 ± 1.4</td>
<td>4.3 ± 1.4</td>
<td>0.999</td>
</tr>
<tr>
<td>HASBLED score</td>
<td>3.1 ± 1.4</td>
<td>2.9 ± 1.6</td>
<td>3.1 ± 1.4</td>
<td>0.536</td>
</tr>
<tr>
<td>CHF or LVEF &lt;40%</td>
<td>55 (40.7 %)</td>
<td>14 (43.8 %)</td>
<td>41 (39.8 %)</td>
<td>0.687</td>
</tr>
<tr>
<td>Hypertension</td>
<td>114 (84.4 %)</td>
<td>28 (87.5 %)</td>
<td>86 (83.5 %)</td>
<td>0.782</td>
</tr>
<tr>
<td>Age ≥ 75 y</td>
<td>58 (43.0 %)</td>
<td>13 (40.6 %)</td>
<td>45 (43.7 %)</td>
<td>0.786</td>
</tr>
<tr>
<td>Age 65 – 74 y</td>
<td>53 (39.3 %)</td>
<td>12 (37.5 %)</td>
<td>41 (39.8 %)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35 (25.9 %)</td>
<td>9 (28.1 %)</td>
<td>26 (25.2 %)</td>
<td>0.818</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>60 (44.4 %)</td>
<td>16 (50.0 %)</td>
<td>44 (42.7 %)</td>
<td>0.543</td>
</tr>
<tr>
<td>Vascular disease (MI)</td>
<td>17 (12.6 %)</td>
<td>4 (12.5 %)</td>
<td>13 (12.6 %)</td>
<td>1.000</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>62 (45.9%)</td>
<td>17 (53.1 %)</td>
<td>45 (43.7 %)</td>
<td>0.418</td>
</tr>
<tr>
<td>Closing device</td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Amplatzer cardiac plug</td>
<td>94 (69.6 %)</td>
<td>3 (9.4 %)</td>
<td>91 (88.3 %)</td>
<td></td>
</tr>
<tr>
<td>Amulet</td>
<td>35 (25.9 %)</td>
<td>27 (84.4 %)</td>
<td>8 (7.8 %)</td>
<td></td>
</tr>
<tr>
<td>Watchman</td>
<td>6 (4.4 %)</td>
<td>2 (6.3 %)</td>
<td>4 (3.9 %)</td>
<td></td>
</tr>
</tbody>
</table>

## Procedure Related Findings

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Subjects (n = 135)</th>
<th>ICE group (n = 32)</th>
<th>No ICE group (n = 103)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LAAO Indication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OAC contraindicated</td>
<td>92 (68.1 %)</td>
<td>25 (78.1 %)</td>
<td>67 (65.0 %)</td>
<td>0.085</td>
</tr>
<tr>
<td>Stroke or SEE despite OAC</td>
<td>22 (16.3 %)</td>
<td>6 (18.8 %)</td>
<td>16 (15.5 %)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>21 (15.6 %)</td>
<td></td>
<td>20 (19.4 %)</td>
<td></td>
</tr>
<tr>
<td><strong>Type of anesthesia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local anesthesia</td>
<td>33 (24.4 %)</td>
<td>16 (50.0 %)</td>
<td>17 (16.5 %)</td>
<td></td>
</tr>
<tr>
<td>Light sedation</td>
<td>56 (41.5 %)</td>
<td>16 (50.0 %)</td>
<td>40 (38.8 %)</td>
<td></td>
</tr>
<tr>
<td>General anesthesia</td>
<td>46 (34.1 %)</td>
<td>0</td>
<td>46 (44.7 %)</td>
<td></td>
</tr>
<tr>
<td><strong>Procedure time (min)</strong></td>
<td>79.0 ± 29.2</td>
<td>69.9 ± 29.1</td>
<td>81.8 ± 28.7</td>
<td>0.043</td>
</tr>
<tr>
<td><strong>Fluoroscopy time (sec)</strong></td>
<td>799.9 ± 588.3</td>
<td>617.3 ± 463.4</td>
<td>856.7 ± 613.0</td>
<td>0.022</td>
</tr>
<tr>
<td><strong>Radiation dosage (mGy)</strong></td>
<td>1036.5 ± 1064.0</td>
<td>668.9 ± 433.9</td>
<td>1167.7 ± 1179.2</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Procedural success</strong></td>
<td>132 (97.8 %)</td>
<td>32 (100.0 %)</td>
<td>100 (97.1 %)</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Acute procedural complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>1 (0.7 %)</td>
<td>0</td>
<td>1 (1.0 %)</td>
<td>0.258</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Device embolization</td>
<td>3 (2.2 %)</td>
<td>0</td>
<td>3 (2.9 %)</td>
<td></td>
</tr>
<tr>
<td>Air embolization</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Thrombus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Vascular complications</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

With ICE, we could perform LAAO procedure **without general anesthesia** in **shorter time with lesser radiation exposure!!**
Remaining Issues

• How can we improve procedural safety?
  ➡️ Intra-procedural safety and outcome can be improved with intra-cardiac echocardiography (ICE)

➡️ Pre-procedural planning with 3D printed model can improve procedural safety and outcome

• LAAO can accelerate diastolic dysfunction in patients with less remodeled LA

• Who can stop anticoagulation after LAAO?
  ➡️ Needs to be addressed... and more...


Cho IS... Shin SY et al. ESC 2019 poster presentation

Phan QT... Shin SY et al. Cardiol J. May 2. doi: 10.5603/CJ.a2018.0047
TEE vs. 3D CT Simulation

Bias: -0.11 mm (95% CI: -0.93-0.72mm)
TEE vs. 3D CT Simulation

$r=0.544 (p=0.028)$

$r=0.927 (p<0.001)$

Cho IS... Shin SY et al. ESC 2019 poster presentation
Remaining Issues

• How can we improve procedural safety?
  ➞ Intra-procedural safety and outcome can be improved with intra-cardiac echocardiography (ICE)

  ➞ Pre-procedural planning with 3D printed model can improve procedural safety and outcome

• LAAO can accelerate diastolic dysfunction in patients with less remodeled LA

• Who can stop anticoagulation after LAAO?
  ➞ Needs to be addressed... and more...


Cho IS... Shin SY et al. ESC 2019 poster presentation

Phan QT... Shin SY et al. Cardiol J. May 2. doi: 10.5603/CJ.a2018.0047
**PLAATO achieved an adequate seal of the neck of LAA w/o significant effect on the structure of the LA and LUPV**
LAA Exclusion Can Worsen HF

- 47 LAAO vs. 141 Non-LAAO
- Retrospective Difference-in-Different analysis for hemodynamic changes before and after LAAO

<table>
<thead>
<tr>
<th>Variables</th>
<th>LAAC group (n=47)</th>
<th>Non-LAAC group (n=141)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>75.1 ± 9.9</td>
<td>74.7 ± 9.7</td>
<td>0.799</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>20 (42.6%)</td>
<td>60 (42.6%)</td>
<td>1.000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.4 ± 3.8</td>
<td>24.3 ± 3.7</td>
<td>0.953</td>
</tr>
<tr>
<td>Paroxysmal AF (n, %)</td>
<td>13 (27.7%)</td>
<td>34 (24.1%)</td>
<td>0.627</td>
</tr>
<tr>
<td>HAS-BLED score</td>
<td>2.55 ± 1.41</td>
<td>2.23 ± 1.34</td>
<td>0.156</td>
</tr>
<tr>
<td>CHA₂DS₂-VASc score</td>
<td>3.83 ± 1.98</td>
<td>3.32 ± 1.65</td>
<td>0.082</td>
</tr>
<tr>
<td>Labile INR (n, %)</td>
<td>6 (12.8%)</td>
<td>20 (14.2%)</td>
<td>0.807</td>
</tr>
<tr>
<td>Bleeding (n, %)</td>
<td>8 (17.0%)</td>
<td>23 (16.3%)</td>
<td>0.910</td>
</tr>
<tr>
<td>Stroke or TIA (n, %)</td>
<td>21 (44.7%)</td>
<td>49 (34.8%)</td>
<td>0.223</td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>32 (68.1%)</td>
<td>92 (65.2%)</td>
<td>0.722</td>
</tr>
<tr>
<td>Diabetes mellitus (n, %)</td>
<td>6 (12.8%)</td>
<td>21 (14.9%)</td>
<td>0.719</td>
</tr>
<tr>
<td>Congestive heart failure (n, %)</td>
<td>14 (29.8%)</td>
<td>35 (24.8%)</td>
<td>0.502</td>
</tr>
<tr>
<td>Chronic kidney disease (n, %)</td>
<td>5 (10.6%)</td>
<td>13 (9.2%)</td>
<td>0.775</td>
</tr>
<tr>
<td>Vascular diseases (n, %)</td>
<td>7 (14.9%)</td>
<td>14 (9.9%)</td>
<td>0.349</td>
</tr>
</tbody>
</table>

Abbreviations: TEE: tranesophageal echocardiography; LAAC: left atrial appendage closure; BMI: body mass index; INR: international normalized ratio; TIA: transient ischemic attack; AF: atrial fibrillation; bpm: beats per minute; EF: left ventricular ejection fraction;
$E/E'$ Elevation After LAAO

![Graph showing E/e' ratio change after LAAO showing a significant increase with p = 0.028 and DID = +2.25.](image)

- **Baseline** $E/e'$ ratio
- **Endline** $E/e'$ ratio

**LAAC group**
- \( p = 0.028 \)
- \( \text{DID} = +2.25 \)

**non-LAAC group**

References:
Phan QT... Shin SY et al. Cardiol J. May 2. doi: 10.5603/CJ.a2018.0047
More LA Remodeling After LAAO

![Graph showing LAVI (ml/m²) over time for LAAC group and non-LAAC group. The graph indicates a statistically significant increase in LAVI with the LAAC group showing a DID of +5.85 compared to the non-LAAC group. The p-value is 0.011.](image)

Phan QT... Shin SY et al. Cardiol J. May 2. doi: 10.5603/CJ.a2018.0047
The Smaller LA, The Worse

- Smaller LA will experience the worse deterioration of the diastolic function after LAAO.
- Patients with paroxysmal AF without LA enlargement (less remodeled LA) are more likely to experience the worsening of heart failure after LAAO.

Phan QT... Shin SY et al. Cardiol J. May 2. doi: 10.5603/CJ.a2018.0047
Remaining Issues

• How can we improve procedural safety?
  ➤ Intra-procedural safety and outcome can be improved with intra-cardiac echocardiography (ICE)
  ➤ Pre-procedural planning with 3D printed model can improve procedural safety and outcome

• LAAO can accelerate diastolic dysfunction in patients with less remodeled LA

• Who can stop anticoagulation after LAAO?
  ➤ Needs to be addressed... and more...
Switch from OAC to APT / OAC Discontinuation

• No General Rule!
• Timing (6 weeks)
• Procedural outcome
  - Peri-device leakage
  - Endothelialization
• Blood stasis (HF worsening)
• Indication for procedure
Endothelialization vs. Stasis?

Indication for LAAO:
- Recurrent stroke & major bleeding during OAC
- Successful LAAO
- 2 M & 12 M f/u TEE
  → Complete sealing w/o thrombi during single APT
  → Endothelialization completion?

At 18 M after LAAO,
- HF exacerbation during stress cardiomyopathy
  - LVEF 65% → 28%
  - Thrombi on disc surface

At 20 M after LAAO,
- (OAC for 2 M & HF Mx)
  - LVEF 28% → 55%
  - Thrombi disappeared
  - OAC → APT
  - No further thrombotic events up to 36 M after LAAO
General Rule?

- Absolute timing (6 weeks)?
- Procedural outcome
  - Peri-device leakage
  - Endothelialization
- Blood stasis (HF worsening)

→ **Thrombogenicity of blood?**

No General Rule!
Thrombogenicity After Closure

- PFO closure after cryptogenic stroke (n = 24)
- Measure thrombogenicity (prothrombin fragment 1 + 2, TAT III) & platelet activity (P-selectin, CD40)

Enhanced Thrombogenicity – return to baseline 90 days later

Levels of the markers of coagulation and platelet activation at baseline and at 7, 30, and 90 days after transcatheter closure of PFO. A, B, C, D: Levels of prothrombin fragment 1 + 2, TAT III, soluble P-selectin, soluble CD40 ligand, respectively.
Healing Process of Implanted Device

- Explanted ASD or PFO closure device (n = 9)
- Mean interval: \(3.4 \pm 2.4\) years (0.9 – 8.3 years)
- Recurrent thromboembolic events (n = 5)
- Residual shunt/dislocation (n = 3)
- Growing mass on device (n = 1) – hyperplastic tissue formation
Explanted ASD or PFO Devices

Vogt MO et al. *Int J Cardiol.* 2011; 147: 398-404
Hyperplastic Tissue / Thrombi
LAAO Major Indications in EU

Korean national insurance covered indications since 2017

- Generally, acceptable indications?

Alternative to OAC in patients with no increased risk for bleeding

*CHADS2-VASc ≥ 2 but contraindication to OAC*

*CHADS2-VASc ≥ 2 and HAS-BLED ≥ 3*

*Embolic events despite OAC*

*CHADS2-VASc ≥ 2 and end-stage renal failure*

*CHADS2-VASc ≥ 2 and triple anticoagulant therapy*

*CHADS2-VASc ≥ 2 and PVI*
Recurrent ischemic stroke during anticoagulation

M/70
Chief complaint:
Recurrent ischemic stroke
Present illness) Referred via local hospital after t-PA
Past medical history:
Persistent AF with moderate AS, AR, MR (Apixaban 5 mg)
CHA\textsubscript{2}DS\textsubscript{2}-VASc score = 3 (Stroke, Age 65~74)
HASBLED = 1 (Stroke)
s/p Rt. MCA infarction with hemorrhagic transformation (2014)
Rt. ACA unruptured aneurysm with failed intervention – follow-up NS
\begin{itemize}
  \item \textbf{Previously LAAO was recommended, but refused}
\end{itemize}
s/p Stomach cancer (2016, total gastrectomy)
Brain CT

Initial CT $\rightarrow$ Craniectomy & drainage $\rightarrow$ Expired
Elderly patient with recurrent GI bleeding

M/73

Chief complaint)

Recurrent, intractable diverticular bleeding during OAC
(3 recurrent bleeding episodes requires transfusion > 2 units PRBC)

Present illness)

Failed to perform thoracoscopic LAA ligation because of severe pericardial adhesion (Feb. 2019)

Because of recurrent bleeding, OAC discontinued since April, 2019

Past medical history)

CHA$_2$DS$_2$-VASc score = 5

CHF (EF = 46 %), DM, Stroke, Age 65~74

HASBLED = 3 (CKD III, Stroke, Bleeding)

s/p AF ablation by cryoballoon (4 PV – Feb. 2019)
Trans-Esophageal Echocardiography
(14th June 2019, After LMWH 8 days)
Cardiac CT Measurement

Distance: 45.5 mm, 27.6 mm
Area: 9.89 cm²
Avg. Diameter: 34.6 mm
Perimeter: 117 mm

%R-R: 35

36.2 mm

11.9 mm

32.3 mm
3D Simulation – 28/31/34 mm
Decided to Perform LAAO, but…

• **Two months** after OAC discontinuation, in his LAA...
• Pre-procedural anticoagulation with LMWH 7 days

⇒ Postpone procedure after temporary anticoagulation
Take Home Messages

• Non-pharmacologic stroke prevention is still necessary in NOAC era

• Current LAAO technology demonstrated feasibility, but it needs to be improved in terms of safety, efficacy
Thank you for Your Attention

E-mail: theshin04@cau.ac.kr
010-8863-1078