Role of Surgical Maze/Hybrid Approaches

Case Presentation

- 55 yo gentleman
  - Hx of persistent AF
  - CHADs score 1
  - Refractory to medical therapy
  - Failed 2 previous PVI

Disclosure

SentreHeart, Inc
- Consultant
- Equity holder

Clinical success of various ablation techniques for persistent/long-standing persistent atrial fibrillation

Catheter Ablation of Long-Standing Persistent Atrial Fibrillation
5-Year Outcomes of the Hamburg Sequential Ablation Strategy
Roland Richard Tilz, MD, Andreas Rillig, MD, Anna-Maria Thum, Anita Arya, MD, Peter Wohlmuth, Andreas Metzner, MD, Shibu Mathew, MD, Yasuhiro Yoshida, MD, Erik Wissner, MD, Karl-Heinz Kuck, MD, Feifan Ouyang, MD

After the first ablation procedure, sinus rhythm was documented in 41 of 202 (20.3%) patients.

After multiple procedures, sinus rhythm was maintained in 91 of 202 (45.0%) patients.

JACC 2012;60:1921–9.

Case Presentation

- 55 yo gentleman
  - Hx of longstanding AF
  - CHA2DS2-VASc score 1
  - Refractory to medical therapy
  - Failed 2 previous PVI
- How do you treat this patient?
  - Repeat PVI
  - AVJ ablation and pacemaker
  - Surgical MAZE
  - Rate control and OAC therapy; and live with your symptoms
SUCCESS AFTER MAZE PROCEDURE in PERSISTENT AF PATIENTS

Comparison of time-related freedom from AF

What is the difference between PVI and Cox-MAZE Procedure?

Atrial Fibrillation Catheter Ablation versus Surgical Ablation Procedure (FAST): a 2-center randomized clinical trial


Atrial Fibrillation Catheter Ablation versus Surgical Ablation Procedure (FAST): a 2-center randomized clinical trial

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>CA N63</th>
<th>SA N61</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall, 12 mo</td>
<td>23 (36.5%)</td>
<td>40 (65.6%)</td>
<td>P=0.0022</td>
</tr>
<tr>
<td>PAF group</td>
<td>13/37 (35.1%)</td>
<td>31/45 (68.9%)</td>
<td>P=0.0047</td>
</tr>
<tr>
<td>Pers AF group</td>
<td>9/25 (36%)</td>
<td>9/16 (56%)</td>
<td>P=0.3411</td>
</tr>
<tr>
<td>Prior failed CA</td>
<td>14/38 (36.8%)</td>
<td>30/44 (68.2%)</td>
<td>P=0.0089</td>
</tr>
</tbody>
</table>

Procedural Adverse Events of CA and SA

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>CA N63</th>
<th>SA N61</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2 (3.2%)</td>
<td>14 (23.0%)</td>
<td>P=0.001</td>
</tr>
</tbody>
</table>

Convergent Approach

Transdiaphragmatic Pericardiacotic Access

Kiser and Moebye: a-fb.com/convergent-hybrid-procedure

UCSF Subxyphoid Approach

Pabst et al. J Am Coll Cardiol 2012;60:54–61
Case Presentation

- 55 yo gentleman
  - Hx of longstanding AF
  - CHADs score 1
  - Refractory to medical therapy
  - Failed 2 previous PV
- How do you treat this patient?
  - Repeat PVI
  - AVJ ablation and pacemaker
  - Rate control and OAC therapy; and live with your symptoms
  - Surgical MAZE
- LAA ligation and Catheter Ablation 5/2011
  - Remains in sinus rhythm
aMAZE Trial

Hypothesis

- The LAA and adjacent structures are critical in the maintenance of persistent and longstanding persistent AF, and LAA ligation and PVI will decrease the recurrence of AF in patients with persistent and long-standing persistent AF.

LAA exclusion as adjunctive therapy to PVI for the treatment of AF: What is the rationale?

- Elimination of atrial arrhythmias arising from the LAA
- Left atrial debulking/reduction results in decreased left atrial dispersion
- Allows for a more complete ablation procedure

Focal AT from the LAA

LAA Isolation Improves Ablation Outcomes

Left Atrial Appendage: An Underrecognized Trigger Site of Atrial Fibrillation

Di Biase et al., Circulation. 2010;122:109-118

Fibrillating Areas Isolated within the Left Atrium after Radiofrequency Linear Catheter Ablation

Rostock.....Haissaguerre JCE 17:807-812, 2006

LAA ligation converts persistent AF to SR

 Courtesy of David Wilber

LAA closure enables a more complete ablation procedure
Atrial Tachycardias Utilizing the Ligament of Marshall Region Following Single Ring Pulmonary Vein Isolation for Atrial Fibrillation

Kim et al. JACC 36:1324-7, 2000

Localized reentry within the left atrial appendage: arrhythmogenic role in patients undergoing ablation of persistent atrial fibrillation


Protocol Synopsis

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

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

**Design** Prospective, multicenter, RCT (2:1) Bayesian Adaptive Design; 400 – 600 subjects total; ~50 sites

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

**Investigational Tx** LARIAT LAA ligation followed by PVI catheter ablation (separated by >4 weeks)

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

Primary Endpoints

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

**Primary Safety Endpoint** The incidence of significant LARIAT device or procedure-related SAEs occurring within 30 days after the LAA ligation procedure (Performance Goal)
Effectiveness Endpoint Definition

Freedom from episodes of AF > 30 seconds at 12M post-index PVI follow-up, defined as:

- Any episode of AF/AT/AFL > 30 sec
- Documented by 24-hour holter (@ 6 & 12M)
- No requirement for new Class I or III AAD therapy prescribed for AF following the 90-day blanking period
- No catheter ablation procedures post index PVI (aside from ablation for right-sided AFL)

Primary Safety Events

30-day CEC adjudicated LARIAT device- or procedure-related SAEs:

- Serious injury to cardiac / related structure requiring surgical intervention
- Bleeding
  - ≥ 2 units PRBC administered in post-op day 1 or 2 period
  - Organ / structure injury requiring intervention
  - Fatal
- Pericarditis, hemothorax and / or pneumothorax requiring surgical treatment
- Vascular injury requiring surgical treatment / hospital admission or PRBC transfusion
- Pseudoaneurysm / Arteriovenous fistula on imaging or direct visualization
- Pericardial effusions requiring surgical intervention

Primary Endpoint Assumptions

- Effectiveness Endpoint (Superiority)
  - Powered to detect an absolute difference of 15% between treatment and control
  - Max sample size allows for observed clinically significant difference of 10% as statistically significant
- Primary Safety Endpoint (Performance Goal)
  - Compared against a prospectively defined performance goal (PG) of 10%
    - Expected rate of 6% w/ statistical margin
Understanding the Trial Format

• Study conducted in two stages:
  – Initial (Stage 1) followed by a pivotal stage (Stage 2)
  – All patients from both stages will be included in the primary analysis
• Interim data review of first 100 patients enrolled with 30-day follow-up will be reviewed Data Monitoring Committee (DMC) for endorsement to expand
• Enrollment will continue to a maximum of 175 subjects during Stage 1 analysis and review

Expansion: Stage 1 → 2

Expansion Rules – aligned with futility rules in the interim analyses
• 30-day primary safety endpoint rate: futility bound probability <0.025
• Corresponds to approximately 9 or fewer safety events in the first 67 LARIAT patients and
• Data Monitoring Committee review of overall safety and performance (including closure) identifies no significant issues or trends of concern

Participating Centers (Stage 1)

amaze Participating Centers

S. Mittal, MD
Valley Heart

E. Altman, MD
Southside, North Shore

N. Badhwar, MD
UCSF

L. Chandhok, MD
Bryn Mawr

C. Ellis, MD
Vanderbilt

D. Gibson, MD
Scripps

D. Wilber, MD
Loyola

B. Gidew, MD
Cottage, Santa Barbara

Lakkireddy, MD
KUMC

A. Lin, MD
Northwestern

M. Mansour, MD
MGH

A. Rasekh, MD
Baylor/St. Luke’s

D. Tschopp, MD
Austin Heart

Clinical trials.gov identifier: NCT02517397
Notable Secondary Endpoints

• LARIAT Technical Success
  – Successful placement of the LARIAT System pre-tied suture around the LAA to achieve effective LAA ligation
  – Defined as ≤ 1 ± 1mm diameter residual communication w/ LA
  – Assessed by TEE color Doppler, confirmed by Imaging Core Lab immediately post LARIAT (acute), 30-45D post LARIAT and 12M post-PVI

• 30D post PVI MAE*
• Stroke, systemic embolism +/- death of any cause post PVI*
• Freedom from AF/AT/AFL recurrence > 30 sec following 90 day blanking period with or without AAD
• Incidence of reintervention (i.e. catheter or surgical ablation) for recurrence at 12M post-index PVI
• Incidence of DC conversions, re-intervention for recurrence & cardiac hospitalizations at 12M post-index PVI

*adjudicated by CEC

Bipolar recordings

Unipolar recordings

Han et al., Heart Rhythm 2014

Catheter Ablation of Long-Standing Persistent Atrial Fibrillation
5-Year Outcomes of the Hamburg Sequential Ablation Strategy

Roland Richard Tilz, MD, Andreas Rillig, MD, Anna-Maria Thum, Anita Arya, MD, Peter Wohlmuth, Andreas Hetzner, MD, Shibu Mathew, MD, Yasuhiro Yoshiga, MD, Erik Wissner, MD, Karl-Hans Kuck, MD, Feifan Ouyang, MD

After the first ablation procedure, sinus rhythm was documented in 41 of 202 (20.3%) patients.

After multiple procedures, sinus rhythm was maintained in 91 of 202 (45.0%) patients.

JACC 2012;60:1921–9.
**LAALA-AF Registry AA**

- Prospective observational study
- Two groups of persistent AF patients:
  - LAA ligation with LARIAT plus PVI
  - Age and gender matched with PVI only
- Total of 138 patients with 69 LARIAT pts

**Procedural Details**

- LAA Ligation N=69
- LAA Ligation N=69
- Follow up N=138

- LARIAT Group N=69
- PVI Ablation N=69

- 2-3 and 12 month clinic visit
- Hx, Physical, 12 lead EKG, CIED interrogation
- 2 mo non-looping event monitors
- 24hr pads, 104 at ens: 12mo

- Pts offered re-do ablation if recurrent AF >2mo

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**Left Atrial Appendage Ligation and Ablation for Persistent Atrial Fibrillation (LAALA-AF Registry)**


* University of Kansas Hospital and Medical Center, Kansas City, KS
** University of California at San Francisco, San Francisco, CA
† Texas Heart Institute, Houston, TX
‡ Texas Cardiac Arrhythmia Institute, Austin, TX
§ Texas Cardiac Arrhythmia Institute, Austin, TX

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**Left Atrial Appendage : An Underrecognized Trigger Site of Atrial Fibrillation**

Di Biase et al., Circulation. 2010;122:109-118

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**LAA Isolation Improves Ablation Outcomes**

**Left Atrial Appendage : An Underrecognized Trigger Site of Atrial Fibrillation**

**Group I – Std BOX Procedure (n=43)**
**Group II – Std BOX Proc w LAA focal ablation (n=56)**
**Group III – Std BOX Proc w LAA electrical Isolation (n=167)**

<table>
<thead>
<tr>
<th>AF Type</th>
<th>P value (Groups 1 vs 2 vs 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMF</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Pers AF</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>LA Pers AF</td>
<td>20 (36%)</td>
</tr>
</tbody>
</table>

Follow Up Months

- Total Recurrence
- Total Recurrence by Type
- Total Recurrence by Type

- 11+2
- 11+2
- 12+2

- 0.910
- <0.001
Ablation Technique

- Pulmonary vein isolation using double transseptal puncture.
- Demonstration of entrance and exit block from the PVs with 20 pole spiral or lasso catheter
- Additional ablation performed at discretion of operator including:
  - Linear LA lines
  - Right atrial flutter lines
  - CFAE ablation

Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Periprocedural</th>
<th>LARIAT Group*</th>
<th>Ablation Only Group*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardial Effusion</td>
<td>1 (1.4%)</td>
<td>1 (1.4%)</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>LARIAT related</td>
<td>1 (1.4%)</td>
<td>N.A.</td>
<td></td>
</tr>
<tr>
<td>Ablation related</td>
<td>0</td>
<td>1 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Groin Hematoma</td>
<td>2 (2.8%)</td>
<td>2 (2.8%)</td>
<td>2 (2.8%)</td>
</tr>
<tr>
<td>LARIAT related</td>
<td>0</td>
<td>N.A.</td>
<td></td>
</tr>
<tr>
<td>Ablation related</td>
<td>2 (2.8%)</td>
<td>2 (2.8%)</td>
<td></td>
</tr>
<tr>
<td>PV Falx</td>
<td>1 (1.4%)</td>
<td>1 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>LARIAT related</td>
<td>0</td>
<td>N.A.</td>
<td></td>
</tr>
<tr>
<td>Ablation related</td>
<td>1 (1.4%)</td>
<td>1 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5.6%</td>
<td>5.6%</td>
<td></td>
</tr>
</tbody>
</table>

*LARIAT group includes LARIAT procedure and staged ablation

Unexpectedly High Incidence of Stroke and Left Atrial Appendage Thrombus Formation after Electrical Isolation of the Left Atrial Appendage for Treatment of Atrial Tachyarrhythmias: An undescribed and under recognized complication of left atrial catheter ablation

Andreas Rillig, MD, Roland R. Tilz, MD, Tina Lin, MD, Christian Heeger, MD, Anita Arya, PhD, Andreas Metzner, MD, Shibu Mathew, MD, Erik Wissner, MD, Hisaki Makimoto, MD, PhD, Peter Wohlmuth, Karl-Heinz Kuck, MD, Feifan Ouyang, MD

- Mechanical standstill
- Thrombus formation

LAA thrombus in 21%, and three patients had a stroke while on OAC

When should you exclude the LAA: Before or After PVI?
Feasibility and Safety of Combined PVI and LAA closure

Ablation for Atrial Fibrillation in Combination With Left Atrial Appendage Closure: First Results of a Feasibility Study
Martin J. Swaans, MD; Martijn C. Post, MD, PhD; Benno J.W.M. Rensing, MD, PhD; Lucas V.A. Boersma, MD, PhD
J Am Heart Assoc. 2012

Combined catheter ablation and left atrial appendage closure as a hybrid procedure for the treatment of atrial fibrillation
Europace 2015

<table>
<thead>
<tr>
<th>Patient</th>
<th>Device</th>
<th>Size</th>
<th>Time from LAA-closure to LA-ablation (days)</th>
<th>PAF/PersAF</th>
<th>Previous LA-ablation Index procedure</th>
<th>Follow-up: Device related complications assessed by TEE (days)</th>
<th>Follow-up: AT/AF-recurrence (longest follow-up, days)</th>
<th>Follow-up: Clinical complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ACP</td>
<td>22mm</td>
<td>234</td>
<td>PAF -</td>
<td>CPVI</td>
<td>0 (759)</td>
<td>0 (622)</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>WATCHMAN</td>
<td>33mm</td>
<td>182</td>
<td>PAF</td>
<td>CPVI</td>
<td>CPVI</td>
<td>0 (778)</td>
<td>1 (778)</td>
</tr>
<tr>
<td>3</td>
<td>WATCHMAN</td>
<td>21mm</td>
<td>133</td>
<td>PAF -</td>
<td>CPVI</td>
<td>0 (464)</td>
<td>0 (466)</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>WATCHMAN</td>
<td>24mm</td>
<td>105</td>
<td>PersAF</td>
<td>CPVI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>WATCHMAN</td>
<td>24mm</td>
<td>41</td>
<td>PAF -</td>
<td>CPVI</td>
<td>0 (187)</td>
<td>0 (188)</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>WATCHMAN</td>
<td>27mm</td>
<td>92</td>
<td>PAF</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>WATCHMAN</td>
<td>27mm</td>
<td>756</td>
<td>PersAF</td>
<td>CPVI and LAA-isolation via ablation of anterior and mitral isthmus line</td>
<td>Re-isolation of LAA via mitral isthmus line</td>
<td>0 (1006)</td>
<td>0 (1006)</td>
</tr>
<tr>
<td>8</td>
<td>WATCHMAN</td>
<td>27mm</td>
<td>63</td>
<td>PersAF</td>
<td>-</td>
<td>Ablation of CFAEs in CS and LA, anterior line and mitral isthmus line</td>
<td>Thrombus</td>
<td>1 (673)</td>
</tr>
</tbody>
</table>

Heeger, ...Tilz, Heart Rhythm, accepted for publication

PVI and LAA electrical isolation should be done before LAA closure with an LAA implant

Sick et al., JACC 2007

CTA of Watchman device

Courtesy of DJ Lakkireddy
Does left atrial appendage closure improve the success of pulmonary vein isolation? Results of a randomized clinical trial


The Effects of LAA Ligation on LAA Electrical Activity

Frederick T. Han M.D.*, Krzysztof Bartus M.D., Ph.D.*, Dhanunjaya Lakkireddy, M.D., Francia Kiessel, M.D., Jakob Bednarek, M.D., Ph.D., Boguslaw Kapelak, M.D., Ph.D., Magdalena Bartus, Ph.D.*, Nish Badhwar M.B.B.S., FHRSA, Mathew Earnest, M.D., Miguel Valderrabano, M.D., Randall J. Lee M.D., Ph.D.**, N = 30

The Effects of Endoepicardial Percutaneous Left Atrial Appendage Ligation on Arrhythmia Burden in Patients with Atrial Fibrillation

Afzal et al., Heart Rhythm 2015
Sequential Percutaneous LAA ligation and pulmonary vein isolation in patients with persistent AF: Initial results of a feasibility study

Nitish Badhwar, Dhanunjaya Lakkireddy, Mitsuharu Kawamura, Frederick T. Han, Sivaraman K. Iyer, Brian S. Moyers, Thomas A. Dowland, Chris Woods, Ryan Ferrell, Jayanth Nath, Mathew Earnes, Randall J. Lee

![Graph showing P wave dispersion before and after LAA ligation.](image1)

LAA ligation results in a permanent transmural lesion

Bartus et al., Circ Arrhythmia 7:764-767, 2014

LAA closure enables a more complete ablation procedure

Kim et al. JACC 36:1324-7, 2000

Ligament of Marshall

**Recurrent-AF (n=1)**

**SR (n=9)**