



Effect of Empirical Left Atrial Appendage
Isolation on long-term procedure outcome in
patients with Long-Standing Persistent AF
undergoing Catheter Ablation:
Results from the **BELIEF** Randomized Trial

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DECLARATION OF INTEREST

- I am a consultant for Biosense Webster, Srteretaxis and St Jude Medical. I received speaker honoraria/travel from Biotronik, Medtronic, Boston Scientific and Epi EP



Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients with Long-standing Persistent AF undergoing Ablation: Results from the **BELIEF** Randomized Trial

ClinicalTrials.gov Identifier:
NCT01362738

Luigi Di Biase, J. David Burkhardt, MD, Prasant Mohanty, Sanghamitra Mohanty, , Javier E. Sanchez, Chintan Trivedi, Mahmut Güne_, Yalçın Göko•lan, Carola Gianni, Rodney P. Horton, G. Joseph Gallinghouse, Shane Bailey, Jason D. Zagrodzky, Steven C. Hao, Richard H. Hongo, Salwa Beheiry, Pasquale Santangeli, Michela Casella, Antonio Dello Russo, Amin Al-Ahmad, Patrick Hranitzky, Dhanujaya R. Lakkireddy, Claudio Tondo, **Andrea Natale**.

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DISCLOSURES

I am a consultant for

- ✓ Biosense Webster
- ✓ Stereotaxis
- ✓ St Jude Medical

I received speaker honoraria/travel from

- ✓ Atricure
- ✓ Biotronik
- ✓ Boston Scientific
- ✓ Medtronic

BACKGROUND

Long standing persistent (LSP) atrial fibrillation (AF) is the most challenging type of AF to treat with catheter ablation.

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Heart Rhythm Disorders

Catheter Ablation of Long-Standing Persistent Atrial Fibrillation

5-Year Outcomes of the Hamburg Sequential Ablation Strategy

Roland Richard Titz, MD, Andreas Rillig, MD, Anna-Maria Thum, Anita Arya, MD, Peter Wohlmuth, Andreas Metzner, MD, Shibu Mathew, MD, Yasuhiro Yoshiga, MD, Erik Wissner, MD, Karl-Heinz Kuck, MD, Feifan Ouyang, MD
Hamburg, Germany

Objectives This study describes the 5-year efficacy of catheter ablation for long-standing persistent atrial fibrillation (LS-AF).

Background Long-term outcome data after catheter ablation for LS-AF are limited.

Methods Long-term follow-up of 56 months (range 49 to 67 months) was performed in 202 patients (age 61 ± 9 years) who underwent the sequential ablation strategy for symptomatic LS-AF. Initial ablation strategy was circumferential pulmonary vein isolation (PVI). Additional ablation was performed only in acute PVI nonresponder, if direct current cardioversion failed after PVI.

Results 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, including 24 patients receiving antiarrhythmic drugs. In 105 patients, PVI was the sole ablative therapy. 49 (46.7%) of those patients remained in sinus rhythm during follow-up. Patients with a total AF duration of <2 years had a significantly higher ablation success rate than patients whose AF duration was >2 years (76.5% vs. 42.2%, respectively; $p = 0.033$). Persistent AF duration (hazard ratio: 1.09 [95% confidence interval: 1.04 to 1.13]; $p < 0.001$) independently predicted arrhythmia recurrences, and acute PVI responders had a reduced risk of relapse (hazard ratio: 0.57 [95% confidence interval: 0.41 to 0.78]; $p < 0.001$) after the first ablation.

Conclusions During 5-year follow-up, single- and multiple ablation procedure success was 20% and 45%, respectively, for patients with LS-AF. For patients with a total AF duration of <2 years, the outcomes were favorable. (J Am Coll Cardiol 2012;60:1921-9) © 2012 by the American College of Cardiology Foundation

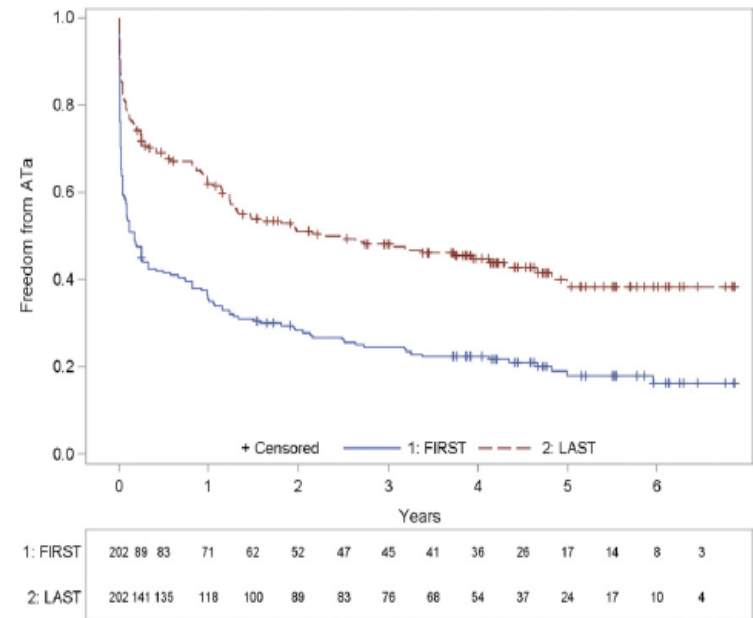


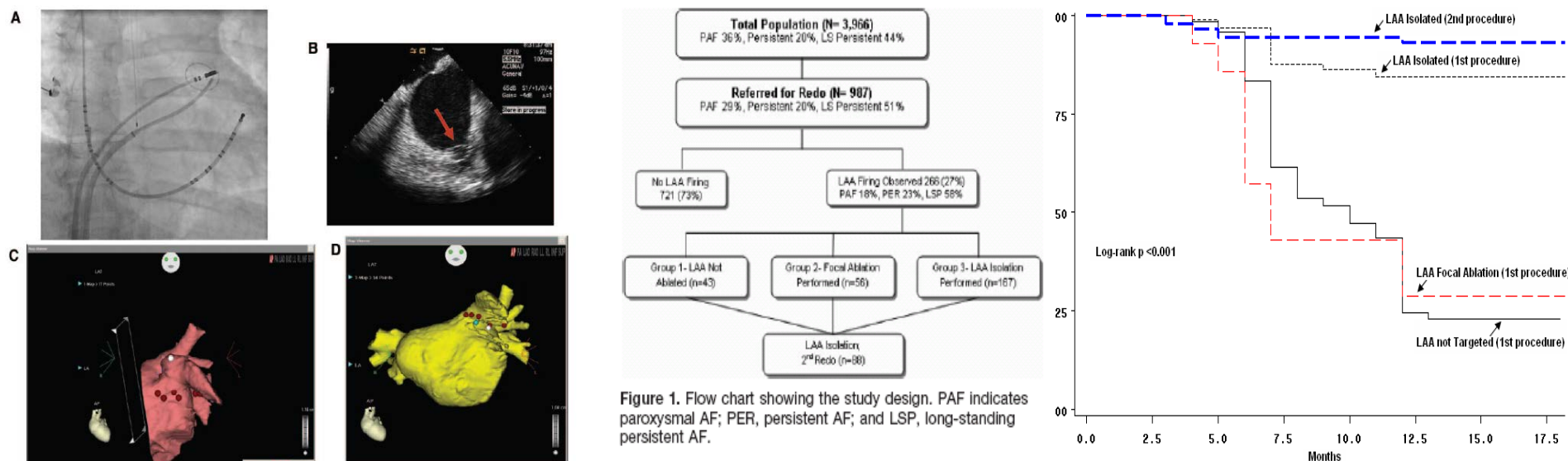
Figure 3 Single and Multiple Procedure Outcomes

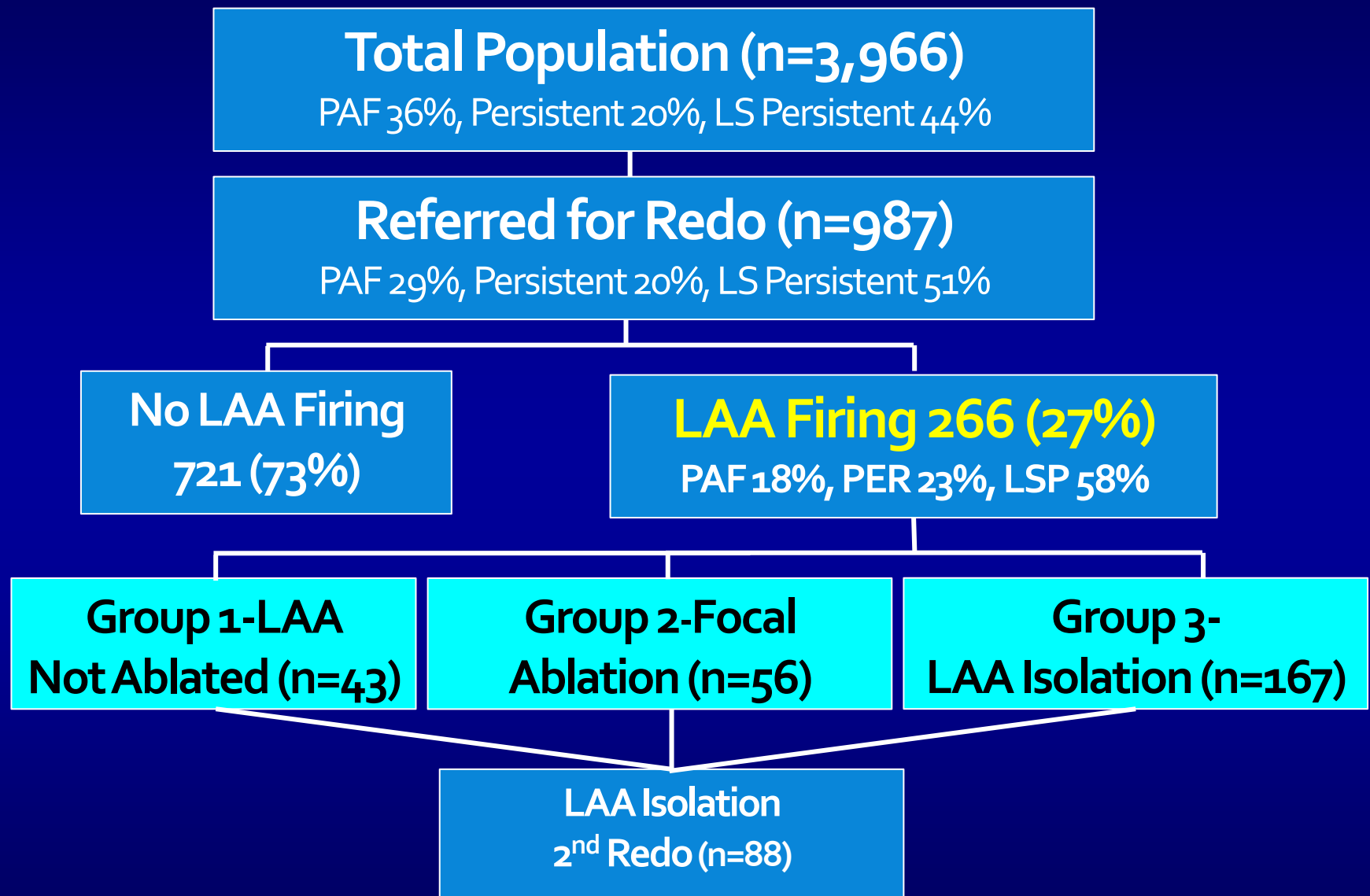
BACKGROUND

- Several studies have shown that in addition to pulmonary vein (PVs) isolation other non PVs areas may be the source of initiation and maintenance of atrial fibrillation in patients.
- The most common sites are: the superior vena cava, the ligament of Marshall, the coronary sinus, the crista terminalis, the left atrial posterior wall and the left atrial appendage.

Left Atrial Appendage : An Underrecognized Trigger Site of Atrial Fibrillation

Luigi Di Biase, J. David Burkhardt, Prasant Mohanty, Javier Sanchez, Sanghamitra Mohanty, Rodney Horton, G. Joseph Gallinghouse, Shane M. Bailey, Jason D. Zagrodzky, Pasquale Santangeli, Steven Hao, Richard Hongo, Salwa Beheiry, Sakis Themistoclakis, Aldo Bonso, Antonio Rossillo, Andrea Corrado, Antonio Raviele, Amin Al-Ahmad, Paul Wang, Jennifer E. Cummings, Robert A. Schweikert, Gemma Pelargonio, Antonio Dello Russo, Michela Casella, Pietro Santarelli, William R. Lewis and Andrea Natale



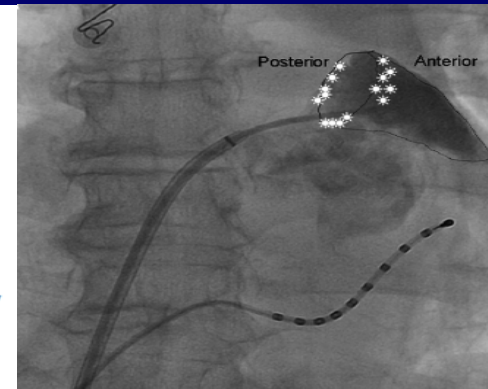


Di Biase et al. Circulation. 2010;122:109-118.

EVIDENCE of the LAA as a TRIGGER for AF/AT

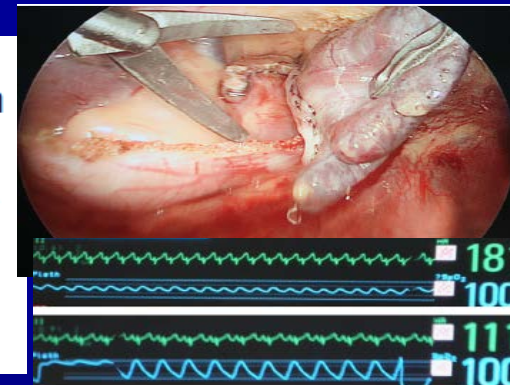
Localized reentry within the left atrial appendage: arrhythmogenic role in patients undergoing ablation of persistent atrial fibrillation

Mélèze Hocini, MD, Ashok J. Shah, MD, Isabelle Nault, MD, Prashanthan Sanders, MBBS, PhD, Matthew Wright, MBBS, PhD, Sanjiv M. Narayan, MD, FACC, Yoshihide Takahashi, MD, Pierre Jaïs, MD, Seiichiro Matsuo, MD, Sébastien Knecht, MD, Frédéric Sacher, MD, Kang-Teng Lim, MD, Jacques Clémenty, MD, Michel Haïssaguerre, MD



Management of focal atrial tachycardias originating from the atrial appendage with the combination of radiofrequency catheter ablation and minimally invasive atrial appendectomy

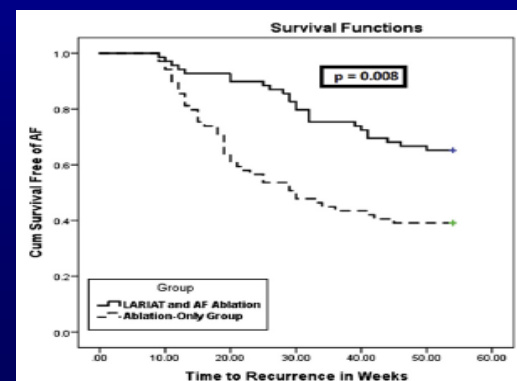
Xiao-gang Guo, MD,* Jin-lin Zhang, MD,[†] Jian Ma, MD,* Yu-he Jia, MD,* Zhe Zheng, MD,[‡] Hong-yue Wang, MD,[§] Xi Su, MD,[†] Shu Zhang, MD, FHRS*



Left Atrial Appendage Ligation and Ablation for Persistent Atrial Fibrillation

The LAALA-AF Registry

Dhanunjaya Lakkireddy, MD,* Arun Sridhar Mahankali, MD,* Arun Kanmanthareddy, MD,* Randall Lee, MD,[†] Nitish Badhwar, MD,[‡] Krzysztof Bartus, MD, PhD,[‡] Donita Atkins, BSN,* Sudharani Bommana, MPhil,* Jie Cheng, MD, PhD,[§] Abdi Rasekh, MD,[§] Luigi Di Biase, MD, PhD,^{||} Andrea Natale, MD,^{||} Jayant Nath, MD,* Ryan Ferrell, MD,* Matthew Earnest, MD,* Yeruva Madhu Reddy, MD*



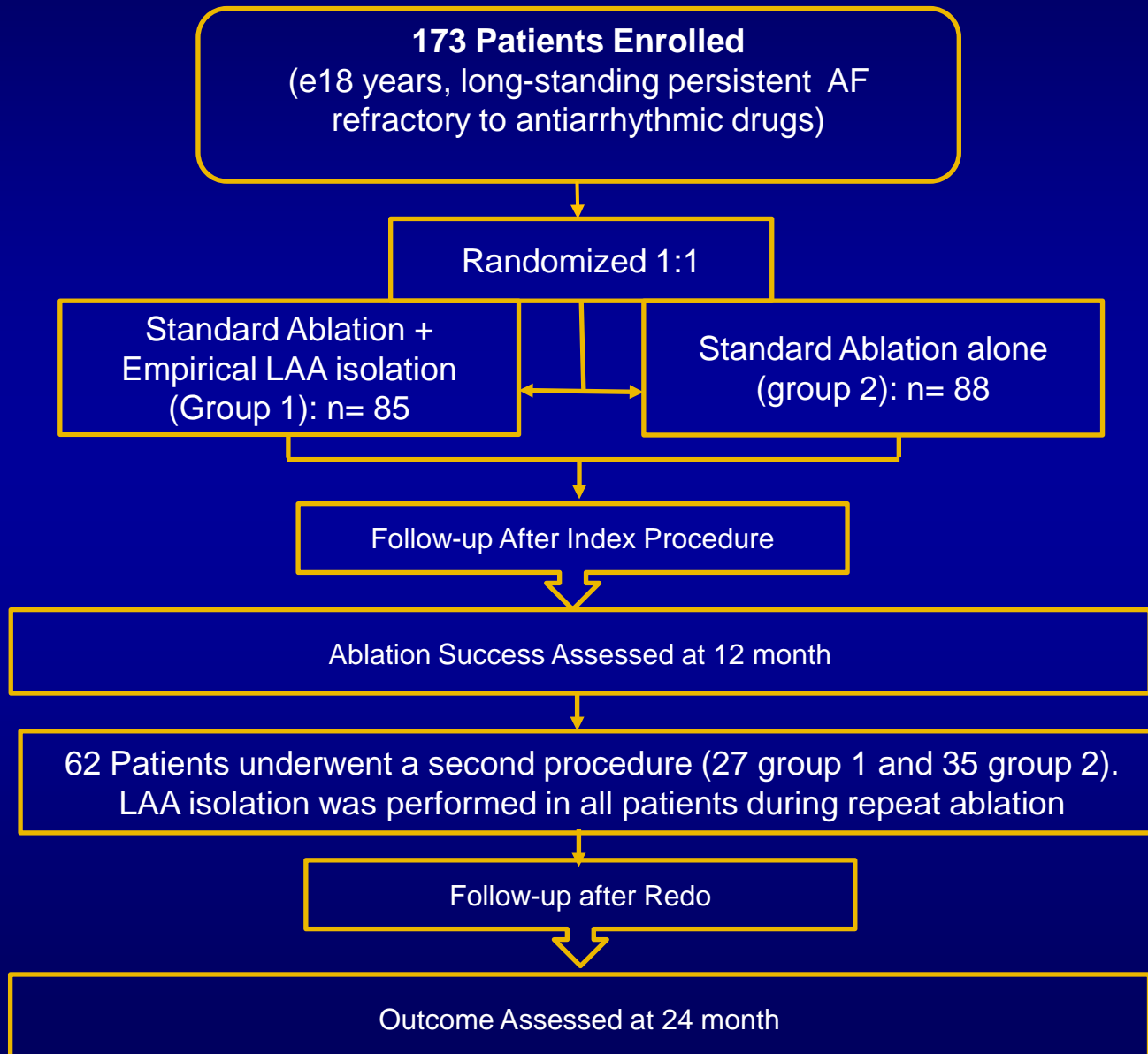
AIM

We sought to assess whether in patients with Long Standing Persistent AF the **EMPIRICAL ELECTRICAL ISOLATION** of the left atrial appendage (**LAA**) in addition to extensive PV antrum and triggers ablation could improve freedom from AF/AT at follow up in a multicenter randomized trial.

Methods

- This was a randomized, parallel-group study assessing whether empirical isolation of the LAA in addition to an extensive standard ablation, could improve the freedom from atrial arrhythmia in LSP AF patients
- Power Calculation: The study had 80% power to detect at least 20% difference in success rate (50% to 70%) at 12 month follow-up (using log-rank test), with two-sided Type I error of 0.05.
- 173 patients were enrolled and randomly assigned (1:1 ratio) to:
 - Extensive ablation plus **Empirical LAA isolation** (group 1, n=85)
 - Extended PV antrum and non PV triggers ablation (group 2, n=88)
- Patients ≥ 18 years of age, with LSP AF refractory to antiarrhythmic drugs were included in the study

Study Design



Methods

- Primary Endpoint:
 - Recurrence of AF/AT lasting longer than 30 seconds was the primary end point of the study
- Secondary endpoints included:
 - Post-ablation hospitalizations due to heart failure and AF related causes
 - Mortality
 - Incidence of stroke

Results

- Baseline and major clinical characteristics were not different between the groups
- The mean radiofrequency time was 93.1 ± 26.2 and 77.4 ± 29.9 minutes ($p < 0.001$) for group 1 and 2 respectively.
- In group 1, LAA could not be isolated in 11 patients due to technical difficulties
 - Extensive ablation was performed in LAA area with partial isolation of the appendage
- In Group 2, 32(36%) patients showed firing from LAA during isoproterenol test
 - A sustained arrhythmia was observed in 8 (9%) of these patients and LAA was isolated
 - Consistent PACs or non-sustained arrhythmia were observed in the remaining 24 patients and LAA was not isolated

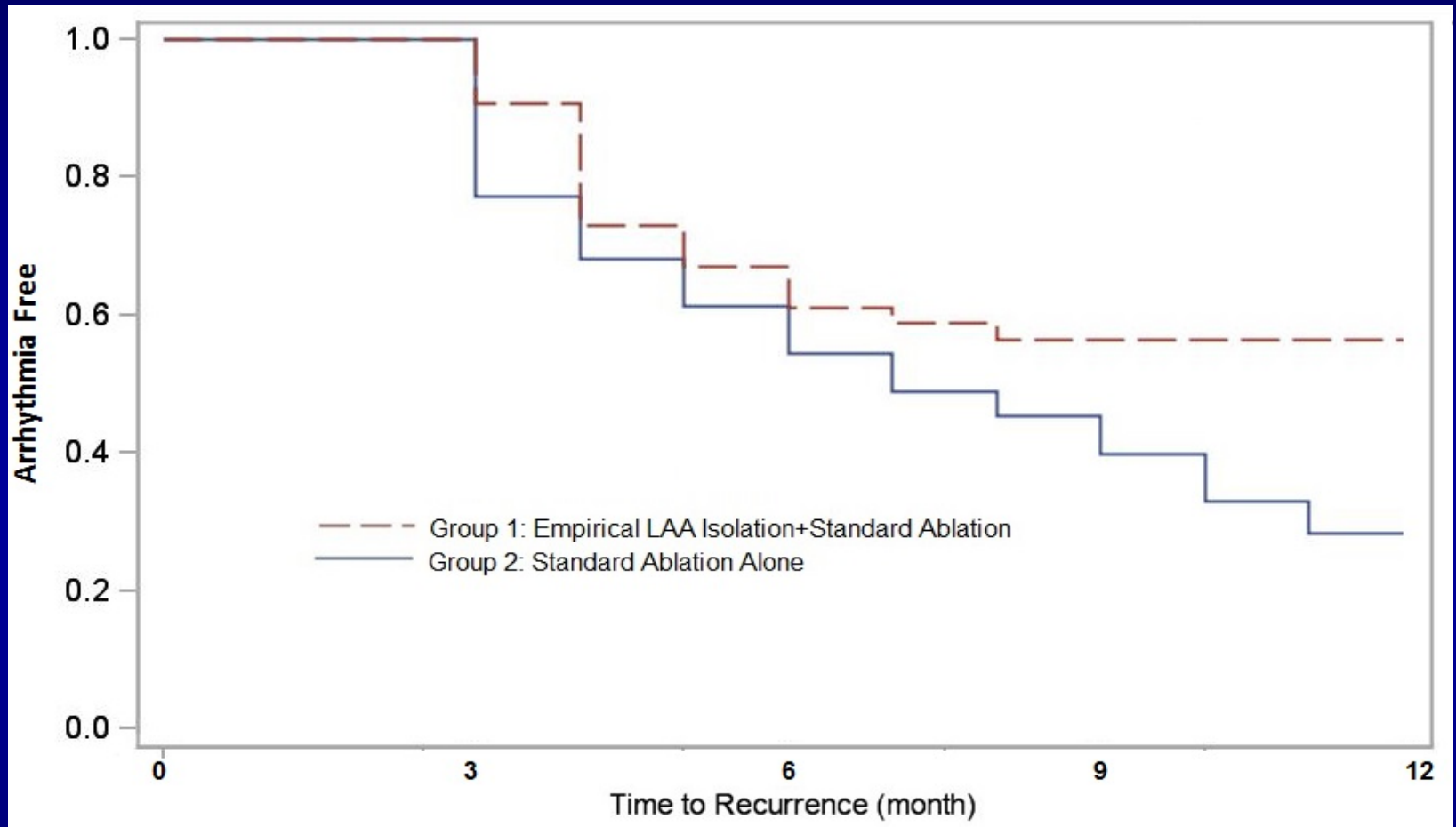
Patient Characteristics (n=173)

	GROUP 1 (N=85)	GROUP 2 (N=88)	P-value
AGE, Yrs	64.25±8.25	63.5±8.7	0.54
Male	75 (88.2%)	73 (83.0%)	0.32
BMI	33.90±8.35	32.5±7.3	0.23
Hypertension	58 (68.2%)	60 (68.2%)	1.00
Diabetes	17 (20.0%)	18 (20.5%)	0.94
Prior CVA/TIA	9 (10.6%)	6(6.8%)	0.38
CHADS2 Score	1.44±1.1	1.30±1.1	0.4
0	18 (21.2%)	22(25.0%)	0.7
1	29 (34.1%)	32 (36.4%)	
e2	38 (44.7%)	34(38.6%)	
LA Diameter, mm	45.8±6.4	46.3±7.0	0.6
LVEF %	53.9±11.3	54.8±10.7	0.63
Dyslipidemia	53 (62.4%)	56 (63.6%)	0.86
CHF	19 (22.4%)	16 (18.2%)	0.5
OSA	18 (21.2%)	20 (22.7%)	0.81
CAD	20 (23.5%)	19 (21.6%)	0.76
No. of AADs	1.8±0.9	2.0±0.8	0.13
Procedure Time (min)	182±62	170±56	0.25
RF Time (min)	93.1±26.2	77.4±29.9	<0.001
Fluoroscopy Time (min)	72±26	66±29	0.15

Results: Arrhythmia Recurrence

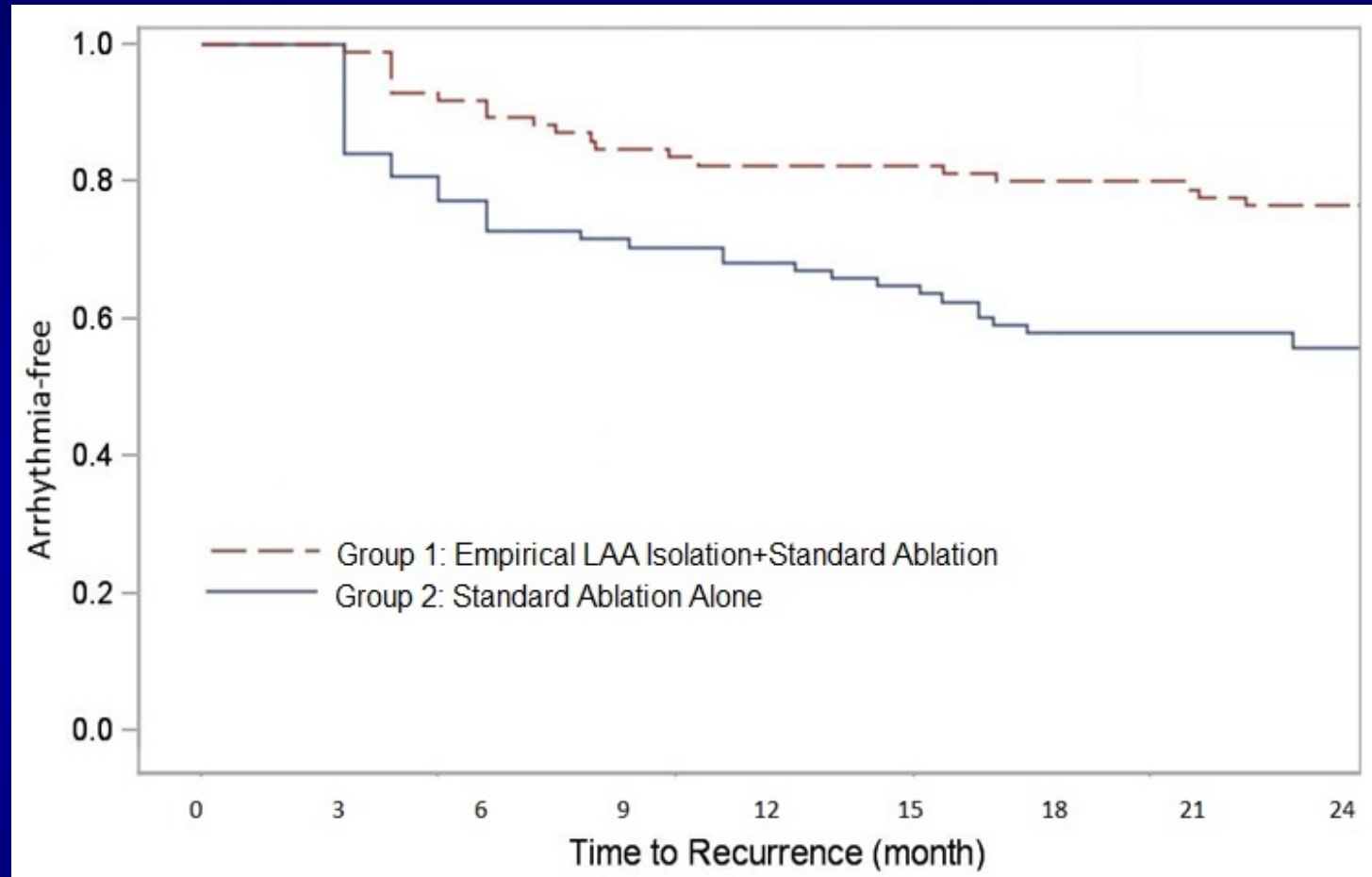
- No patients were lost to follow-up
- At the 12 month follow-up, freedom from recurrence after single procedure was reported in
 - 48(56%) in group 1 and 25(28%) in group 2
 - Log-rank $p=0.001$, unadjusted HR 1.92 (1.3 to 2.9)
- Sixty-two patients (27 group 1 and 35 group 2) underwent a second procedure.
LAA isolation was performed in all patients of either groups during repeat ablation
- After average of 1.3 procedures, success at 24 months follow-up was:
 - 65 (76%) in group 1 and 49 (56%) in group 2
 - Log-rank $p= 0.003$, unadjusted HR 2.24 (1.3-3.8)

Kaplan–Meier curves: single procedure success rate



At the 12 month follow-up, 48(56%) in group 1 and 25 (28%) in group 2 were recurrence-free off-AAD after a single procedure.
(Log-rank $p=0.001$, unadjusted HR 1.92 [1.3 to 2.9]).

Cumulative Overall Success After 1.3 Procedures



The cumulative success after multiple procedures was 65 (76%) in group 1 and 49 (56%) in group 2

ALL THE PATIENTS UNDERWENT LAA ISOLATION
(Log-rank $p=0.003$, unadjusted HR 2.24 [95% CI 1.3-3.8])

Results: Predictor of Recurrence

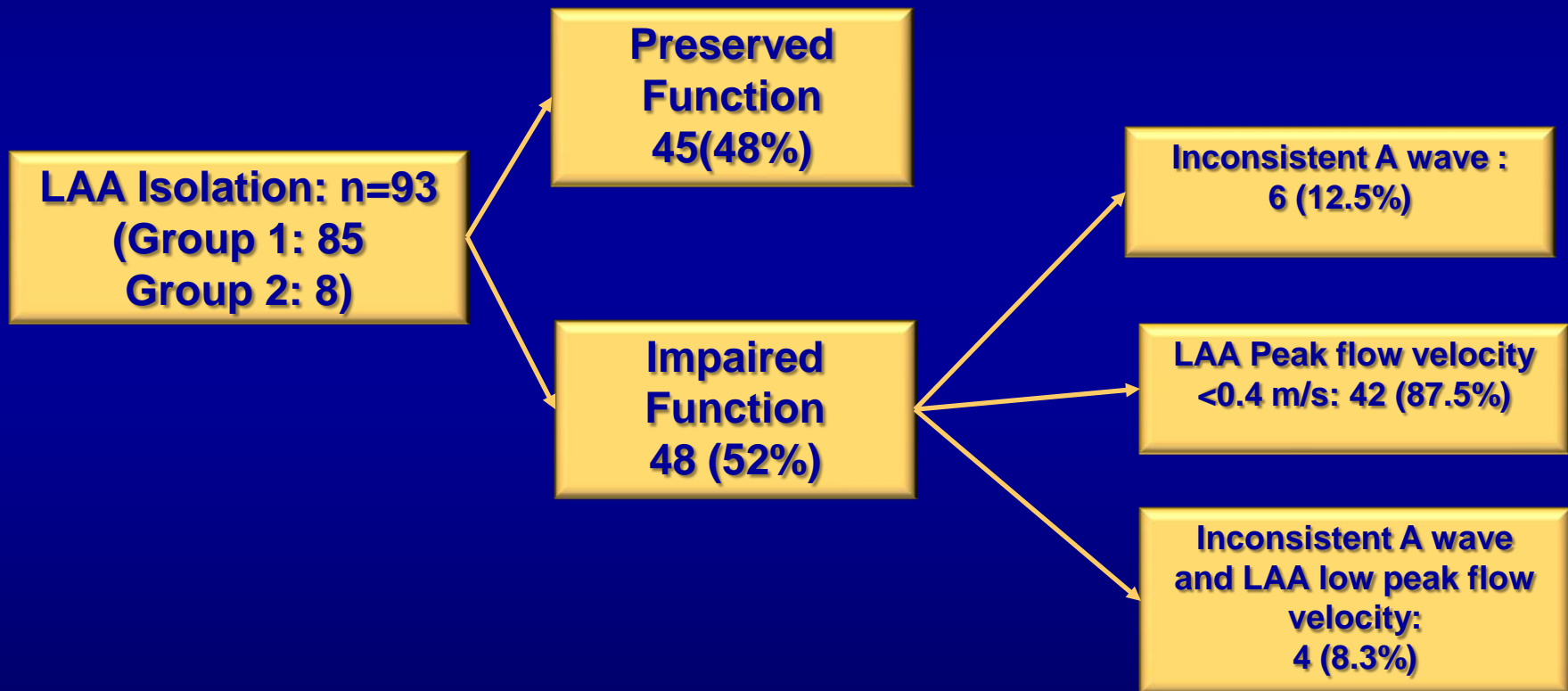
- After adjusting for age, gender, LA diameter in Cox multivariate model
 - Isolation of LAA in addition to standard ablation, was associated with 55% reduction in overall recurrence (HR 0.45 [0.26-0.77], $p=0.004$)

Results: Trans-esophageal echocardiogram (TEE) after a single procedure in patients undergoing LAA isolation

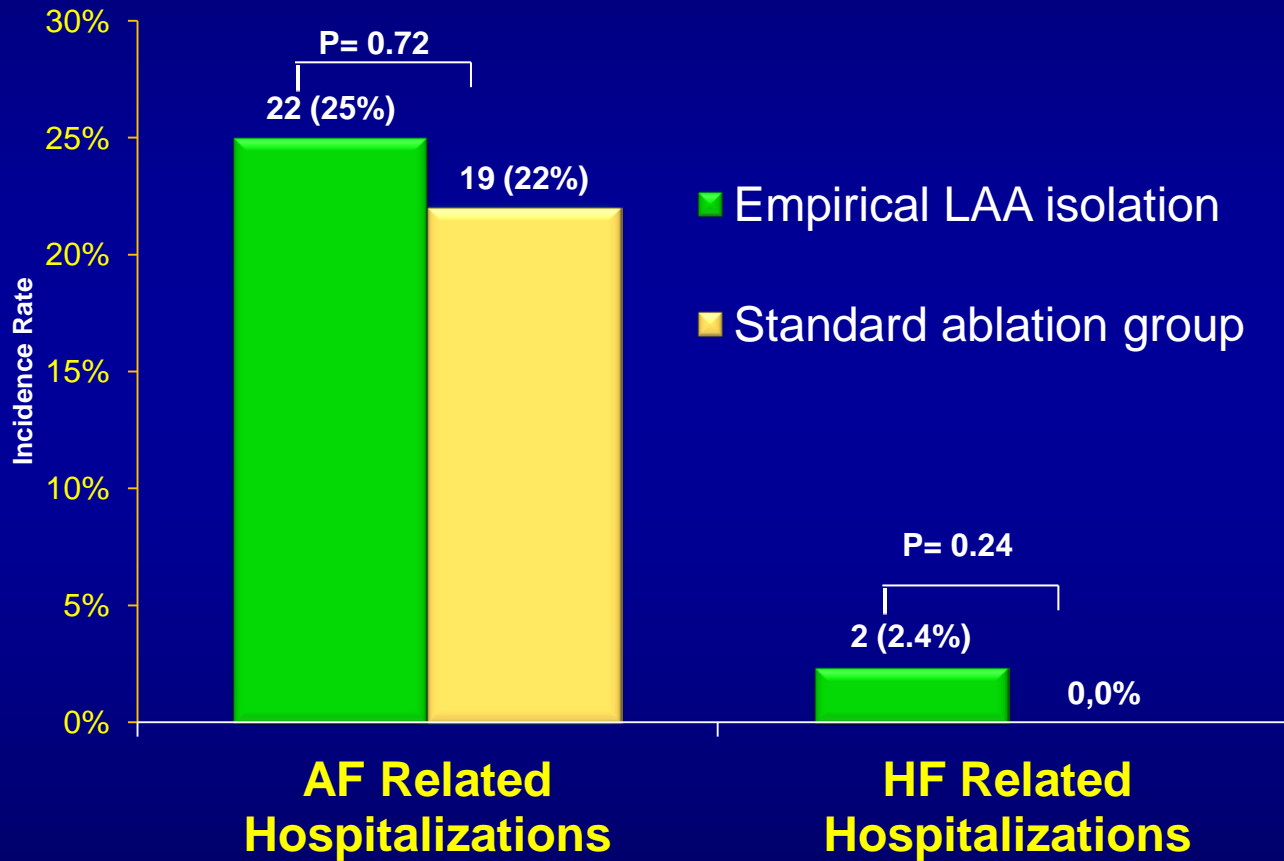
- Patients undergoing LAA isolation received TEE at 6 month follow up, irrespective of their underlying rhythm
- Low peak flow velocity (<0.4 m/s) in the LA appendage was observed in 48 patients
- One LAA thrombus (in patient on OAT with subtherapeutic INR) and one LAA smoke (oral anticoagulant warfarin, INR : 2.24) were detected in the LAA isolation group

Results:

Trans-esophageal echocardiogram (TEE)
after a single procedure in patients undergoing
LAA isolation



Hospitalization



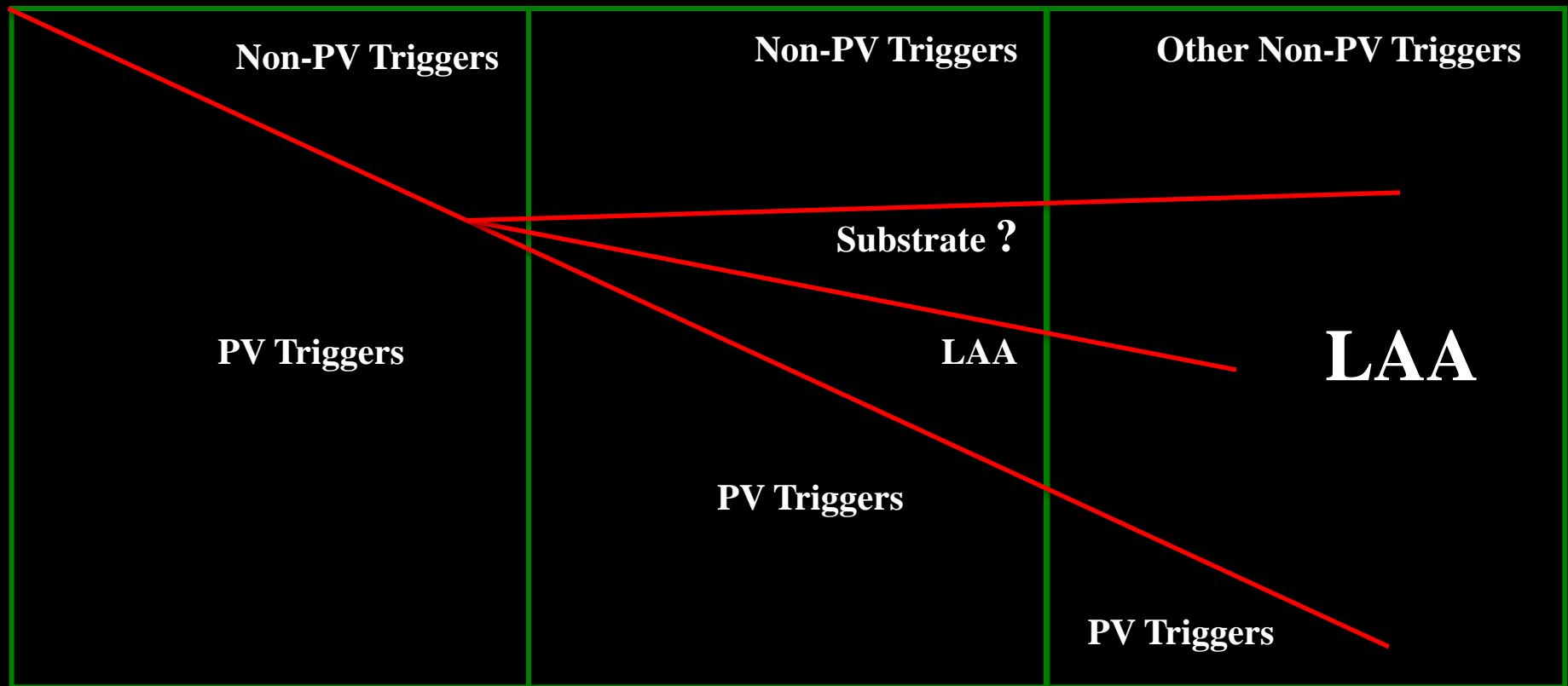
Results: Stroke/TIA and Mortality

- Stroke/TIA:
 - No stroke or TIA was reported in the empirical LAA isolation group,
 - Four (4.5%) patients had stroke in the standard ablation group ($p=0.12$). None of them in patients with LAA isolation
- No deaths occurred during the study period

Results: Peri-Procedural Complications

- Complications:
 - One pericardial effusion occurred in each group ($p=1.0$)
 - One gastrointestinal bleeding was reported in Standard Ablation group ($p=0.49$)

Relative contribution of different ablation targets in the AF disease continuum



Paroxysmal

Persistent

Long-standing persistent

CONCLUSIONS

- The results of this randomized study show that both after a single and redo procedures in patients with **long standing persistent AF**, the ***EMPIRICAL ISOLATION*** of the **LAA** improve the long-term freedom from atrial arrhythmias without increasing complications.
- Future studies examining the physiopathology of these findings are necessary.



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BELIEF

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Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients With Persistent or Long-standing Persistent Atrial Fibrillation Undergoing Catheter Ablation (BELIEF)

This study is currently recruiting participants.

Verified May 2011 by Texas Cardiac Arrhythmia Research Foundation

Sponsor:

Texas Cardiac Arrhythmia Research Foundation

ClinicalTrials.gov Identifier:

NCT01362738

First received: May 26, 2011

Last updated: May 31, 2012

Last verified: May 2011



Optimal Method and Outcomes of Catheter Ablation of Persistent AF: The STAR AF 2 Trial

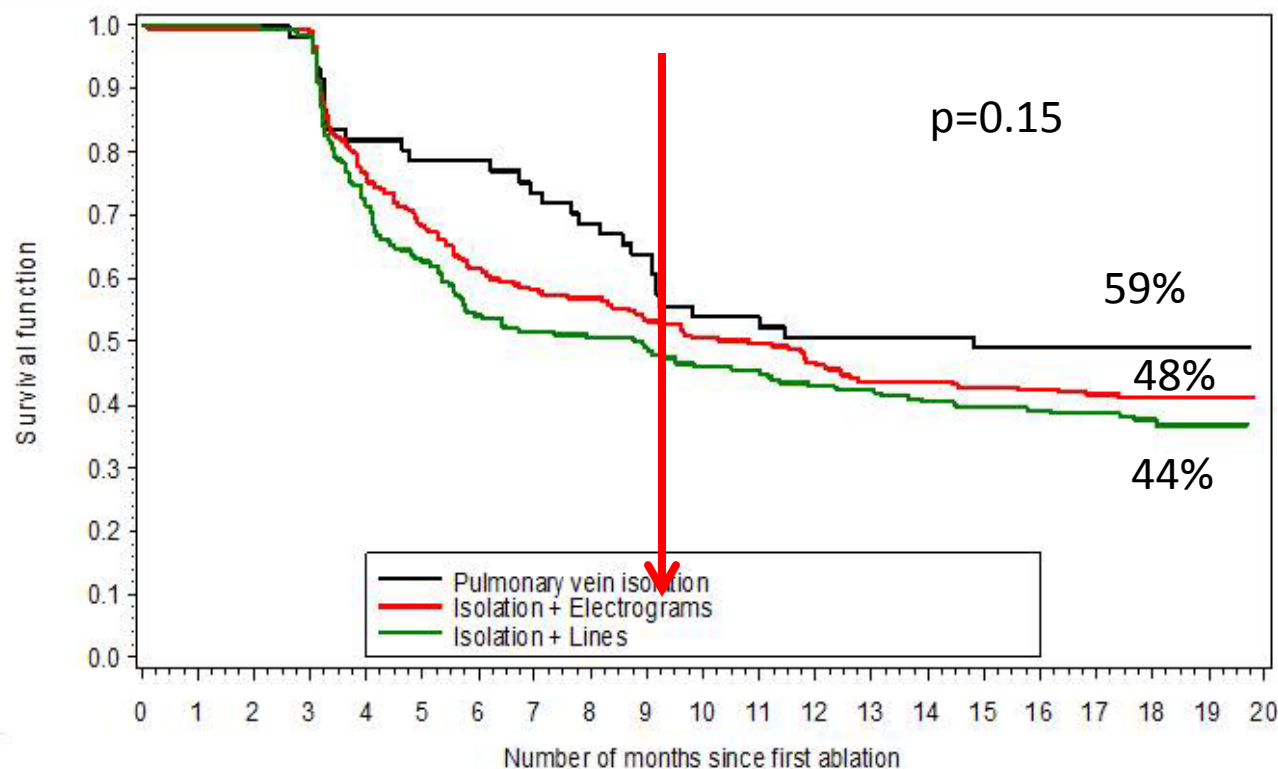
[ClinicalTrials.gov NCT01203748](https://clinicaltrials.gov/ct2/show/study/NCT01203748)

ESC 2014 HOTLINE Presentation



Results - Primary Outcome

Documented AF > 30 seconds after one procedure with or without AAD



No. at Risk

Pulmonary vein isolation	61	60	50	41	36	23
Isolation + Electrograms	244	242	161	137	124	72
Isolation + Lines	244	240	152	133	115	57