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Is STAR AFII The End of the Story?

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Disclosure

Speaker name: Antony Chu MD

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I have the following potential conflicts of interest to report:

Speaker's honorarium for Biosense Webster, Medtronic, Boston Scientific, Abbott, Biotronik

Shareholder – Volta Medical

STAR AF II – What's the Story?



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ORIGINAL ARTICLE

Approaches to Catheter Ablation for Persistent Atrial Fibrillation

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Approach to Catheter Ablation for Persistent AF STAR AFII

BACKGROUND

Catheter ablation is less successful for persistent atrial fibrillation than for paroxysmal atrial fibrillation. Guidelines suggest that adjuvant substrate modification in addition to pulmonary-vein isolation is required in persistent atrial fibrillation.

METHODS

We randomly assigned 589 patients with persistent atrial fibrillation in a 1:4:4 ratio to ablation with pulmonary-vein isolation alone (67 patients), pulmonary-vein isolation plus ablation of electrograms showing complex fractionated activity (263 patients), or pulmonary-vein isolation plus additional linear ablation across the left atrial roof and mitral valve isthmus (259 patients). The duration of follow-up was 18 months. The primary end point was freedom from any documented recurrence of atrial fibrillation lasting longer than 30 seconds after a single ablation procedure.

RESULTS

Procedure time was significantly shorter for pulmonary-vein isolation alone than for the other two procedures ($P < 0.001$). After 18 months, 59% of patients assigned to pulmonary-vein isolation alone were free from recurrent atrial fibrillation, as compared with 49% of patients assigned to pulmonary-vein isolation plus complex electrogram ablation and 46% of patients assigned to pulmonary-vein isolation plus linear ablation ($P = 0.15$). There were also no significant differences among the three groups for the secondary end points, including freedom from atrial fibrillation after two ablation procedures and freedom from any atrial arrhythmia. Complications included tamponade (three patients), stroke or transient ischemic attack (three patients), and atrioesophageal fistula (one patient).

CONCLUSIONS

Among patients with persistent atrial fibrillation, we found no reduction in the rate of recurrent atrial fibrillation when either linear ablation or ablation of complex fractionated electrograms was performed in addition to pulmonary-vein isolation. (Funded by St. Jude Medical; ClinicalTrials.gov number, NCT01203748.)

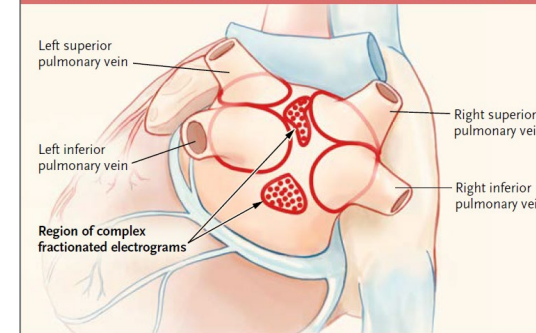
STAR AFII



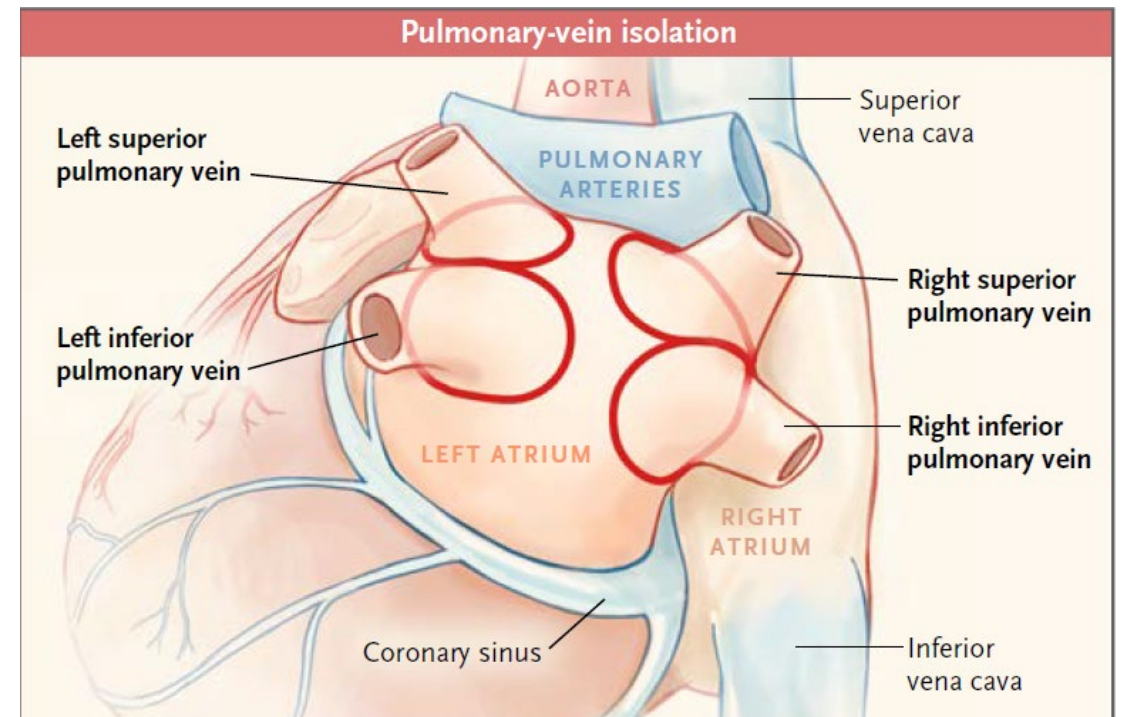
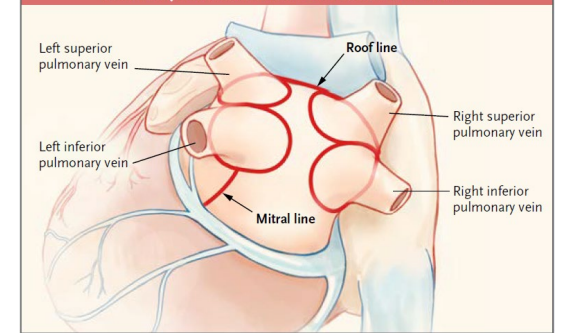
Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Isolation Alone (N = 67)	Isolation plus Electrograms (N = 263)	Isolation plus Lines (N = 259)
Age — yr	58±10	60±9	61±9
Male sex — no. (%)	52 (78)	213 (81)	196 (76)
Ejection fraction — %	55±11	57±10	57±10
Left atrial diameter — mm	44±6	44±6	46±6
Time from first diagnosis of atrial fibrillation — yr	4.3±6.3	4.2±5.0	3.6±4.2
Burden of atrial fibrillation at baseline — hr/mo†	83±36	85±33	80±37
Constant atrial fibrillation for >6 mo — no. (%)	52 (78)	207 (79)	186 (72)
Medical history — no. (%)			
Hypertension	32 (48)	143 (54)	158 (61)
Diabetes	6 (9)	31 (12)	26 (10)
Coronary disease	2 (3)	21 (8)	29 (11)
Stroke or transient ischemic attack	6 (9)	14 (5)	19 (7)
Heart failure	3 (4)	10 (4)	15 (6)
CHADS ₂ score — no. (%)			
0	31 (46)	93 (35)	81 (31)
1	25 (37)	126 (48)	127 (49)
2	6 (9)	31 (12)	29 (11)
>2	5 (7)	10 (4)	19 (7)
Baseline CCS SAF score — no./total no. (%)			
0	2/63 (3)	12/248 (5)	14/243 (6)
1	14/63 (22)	55/248 (22)	53/243 (22)
2	19/63 (30)	79/248 (32)	70/243 (29)
3	24/63 (38)	86/248 (35)	89/243 (37)
4	4/63 (6)	16/248 (6)	17/243 (7)
Baseline medications — no. (%)			
Beta-blocker	43 (64)	148 (56)	160 (62)
Calcium-channel blocker	9 (13)	42 (16)	46 (18)
Cardiac glycoside	8 (12)	39 (15)	39 (15)
Propafenone	2 (3)	2 (1)	7 (3)
Flecainide	8 (12)	32 (12)	28 (11)
Sotalol	3 (4)	13 (5)	15 (6)
Amiodarone	16 (24)	50 (19)	62 (24)
Dronedarone	3 (4)	19 (7)	15 (6)
Dofetilide	0	3 (1)	1 (<1)
Vitamin K antagonist	55 (82)	189 (72)	190 (73)
Oral direct thrombin inhibitor	5 (7)	27 (10)	23 (9)
Acetylsalicylic acid	5 (7)	29 (11)	29 (11)

Pulmonary-vein isolation with ablation of complex fractionated electrograms

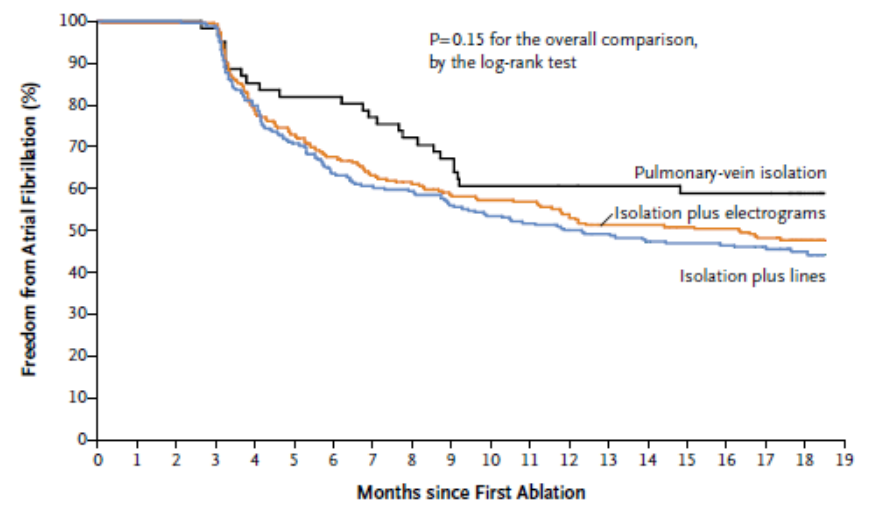


Pulmonary-vein isolation with additional linear ablation





Approach to Catheter Ablation for Persistent AF



No. at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Pulmonary-vein isolation	61	60	50	41	36	23														
Isolation plus electrograms	244	242	161	137	124	72														
Isolation plus lines	244	240	152	133	115	57														

Figure 2. Freedom from Atrial Fibrillation.
 The graph shows Kaplan–Meier estimates of freedom from documented atrial fibrillation more than 30 seconds after a single procedure, with or without the use of antiarrhythmic medications. There were no significant differences between groups ($P=0.15$). Isolation plus electrograms denotes ablation with pulmonary-vein isolation plus additional ablation of complex fractionated electrograms; isolation plus lines refers to ablation with pulmonary-vein isolation plus additional linear ablation.

Table 2. Major Efficacy Outcomes.

Variable	Isolation Alone (N = 61)	Isolation plus Electrograms (N = 244)	Isolation plus Lines (N = 244)	P Value
	number (percent)			
Freedom from documented atrial fibrillation after one procedure, with or without antiarrhythmic drugs	36 (59)	119 (49)	112 (46)	0.15
Freedom from documented atrial fibrillation after one procedure, without antiarrhythmic drugs*	29 (48)	90 (37)	81 (33)	0.11
Freedom from documented atrial arrhythmia after one procedure, with or without antiarrhythmic drugs	30 (49)	100 (41)	90 (37)	0.15
Freedom from documented atrial arrhythmia after one procedure, without antiarrhythmic drugs*	25 (41)	81 (33)	71 (29)	0.08
Freedom from documented atrial fibrillation after two procedures, with or without antiarrhythmic drugs	44 (72)	146 (60)	142 (58)	0.18
Freedom from documented atrial arrhythmia after two procedures, with or without antiarrhythmic drugs	37 (61)	122 (50)	117 (48)	0.24
Documented atrial flutter or tachycardia after one procedure, with or without antiarrhythmic drugs	7 (11)	27 (11)	34 (14)	0.57
Documented atrial flutter or tachycardia after two procedures, with or without antiarrhythmic drugs	7 (11)	32 (13)	29 (12)	0.98
Patients undergoing a second ablation procedure	13 (21)	63 (26)	81 (33)	0.10

Approach to Catheter Ablation for Persistent AF



Table 3. Procedural Adverse Events.*

Adverse Event	Isolation Alone (N = 64)	Isolation plus Electrograms (N = 254)	Isolation plus Lines (N = 250)	Total (N = 568)
	<i>number of events</i>			
Hematoma at access site	2	0	3	5
Arteriovenous fistula or pseudo-aneurysm at access site	0	3	3	6
Pericarditis	0	1	2	3
Fluid overload	0	1	3	4
Sedation-related complication	0	3	5	8
Skin burn	1	0	0	1
Cardiac tamponade	1	0	2	3
Transient ischemic attack or stroke	0	2	1	3
Death due to atrioesophageal fistula	0	1	0	1

- Demographics
 - Unclear BMI/OSA (treatment for obesity/OSA/HTN)
 - Mostly male, CHADS2 0-1, normal LVEF, 76% AF>6 months
- Exclusion Criteria
 - 3 year persistent AF/>6cm LA/PAF
- Energy Source
 - Unipolar RF only
 - No force contact
- Mapping
 - ESI/NAVX
 - Automated CFE software (45% termination)
- Underpowered (1 :4:4) for PVI superiority
- Ablation Targets
 - PVI/EGM software directed/no LAA/No Combined PVI+lines+CFE

PVI alone in Persistent AF – Meta Analysis

Revisiting pulmonary vein isolation alone for persistent atrial fibrillation: A systematic review and meta-analysis

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Revisiting pulmonary vein isolation alone for persistent atrial fibrillation: A systematic review and meta-analysis

BACKGROUND Early studies demonstrated relatively low success rates for pulmonary vein isolation (PVI) alone in patients with persistent atrial fibrillation (PeAF). However, the advent of new technologies and the observation that additional substrate ablation does not improve outcomes have created a new focus on PVI alone for treatment of PeAF.

OBJECTIVE The purpose of this study was to systematically review the recent medical literature to determine current medium-term outcomes when a PVI-only approach is used for PeAF.

METHODS An electronic database search (MEDLINE, Embase, Web of Science, PubMed, Cochrane) was performed in August 2016. Only studies of PeAF patients undergoing a “PVI only” ablation strategy using contemporary radiofrequency (RF) technology or second-generation cryoballoon (CB2) were included. A random-effects model was used to assess the primary outcome of pooled single-procedure 12-month arrhythmia-free survival. Predictors of recurrence were also examined and a meta-analysis performed if ≥ 4 studies examined the parameter.

RESULTS Fourteen studies of 956 patients, of whom 45.2% underwent PVI only with RF and 54.8% with CB2, were included. Pooled single-procedure 12-month arrhythmia-free survival was 66.7% (95% confidence interval [CI] 60.8%–72.2%), with the majority of patients (80.5%) off antiarrhythmic drugs. Complication rates were very low, with cardiac tamponade occurring in 5 patients (0.6%) and persistent phrenic nerve palsy in 5 CB2 patients (0.9% of CB2). Blanking period recurrence (hazard ratio 4.68, 95% CI 1.70–12.9) was the only significant predictor of recurrence.

CONCLUSION A PVI-only strategy in PeAF patients with a low prevalence of structural heart disease using contemporary technology yields excellent outcomes comparable to those for paroxysmal AF ablation.

KEYWORDS Atrial fibrillation; Arrhythmia; Ablation; Pulmonary vein isolation; Cryoballoon

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Revisiting PVI alone for PeAF – Meta Analysis

Table 2 Pulmonary vein isolation only for persistent AF: single-procedure arrhythmia-free survival

Study	RF or CB2	Study design	LsPeAF included	AF ascertainment (other than routine follow-up)	Study name
Lemes 2016 ¹⁷	CB2	Retrospective	✓	3-, 6-, 12-month 24-hour Holter	Lemes 2016
Tscholl 2016 ¹⁸	CB2	Retrospective	×	N/A	Tscholl 2016
Straube 2016 ¹⁹	CB2	Prospective observational	×	3-, 6-, 12-, 18-month 24-hour Holter	Straube 2016
Guhl 2016 ²⁰	CB2†	Retrospective	✓	Event monitor at 6 months	Guhl 2016
Irfan 2016 ²⁸	CB2	Retrospective	✓	3-, 6-, 12-month 24-hour Holter	Irfan 2016
Wynn 2016 ²¹	RF	Randomized trial	×	3-, 6-, 12-month 24-hour Holter	Wynn 2016
Jadidi 2016 ²²	RF	Retrospective	✓	6-, 12-month 24-hour Holter	Jadidi 2016
Pavlovic 2016 ²³	RF	Retrospective	×	3-, 6-, 12-month 7-day Holter	Pavlovic 2016
Khurram 2016 ²⁴	RF	Prospective	✓	Event monitor if symptomatic	Khurram 2016
Koektuerk 2015 ²⁵	CB2	Prospective observational	✓	7-day Holter at 3, 6 months	Koektuerk 2015
Ciconte 2015 ²⁶	RF/CB2	Retrospective	×	3-, 6-, 12-month 24-hour Holter	Ciconte 2015
Vogler 2015 ⁶	RF	Randomized trial	✓	3-, 6-, 9-, 12-month 24- to 72-l Holter	Vogler 2015
Verma 2015 ¹	RF	Randomized trial	✓	Transtelephonic monitor, 3-, 6-, 12-, 18-month 24-hour Holter	Verma 2015
Khan 2011 ²⁷	RF	Prospective observational	×	Transtelephonic monitor, 3-, 6-, 18-month 48-hour Holter	Khan 2011

AF = atrial fibrillation; CB2 = second-generation cryoballoon; IQR = interquartile range; LsPeAF = low sinus pulmonary vein ablation
 *After a 3-month blanking-period. †Majority of patients (12%) had first-generation cryoballoon.

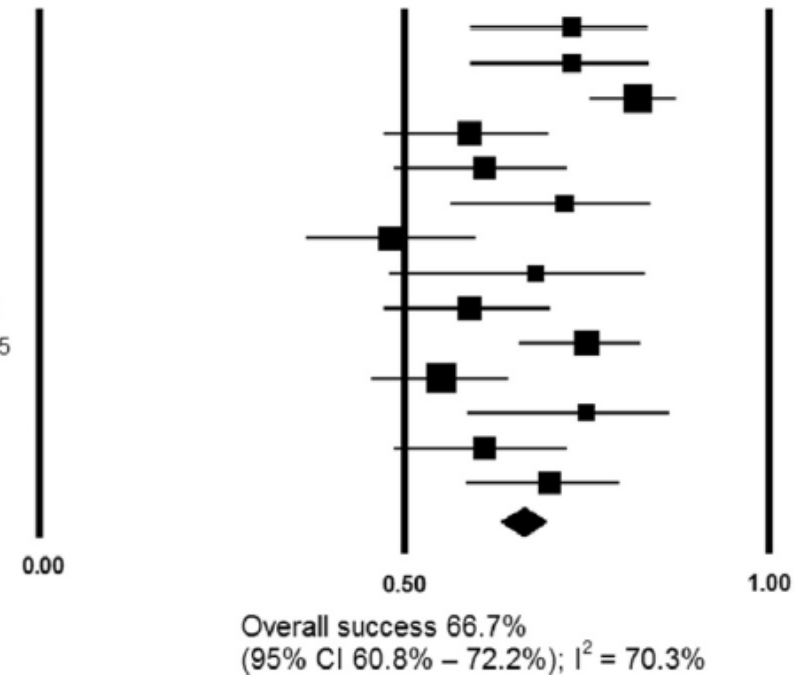


Figure 2 Single-procedure arrhythmia-free survival at 12 months in patients with persistent atrial fibrillation.

- Study Limitations
 - Meta-analysis
 - Only 3 trials RCT (136 patients)
 - Variability in study quality
- Study Conclusions
 - In patients with PeAF and minimal structural heart disease, PVI alone yields 1 year single-procedure arrhythmia free survival of 66.7%
 - Low complication rates
 - Benefits attributed to ongoing technological advances coupled, earlier referral for AF management and risk factor modification

- Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation for both paroxysmal and persistent symptomatic atrial fibrillation (AF).
- Ablation of complex fractionated atrial electrograms (CFAEs) and the creation of various lines of conduction block (linear ablation) in the left atrium are alternative approaches to catheter ablation of AF.

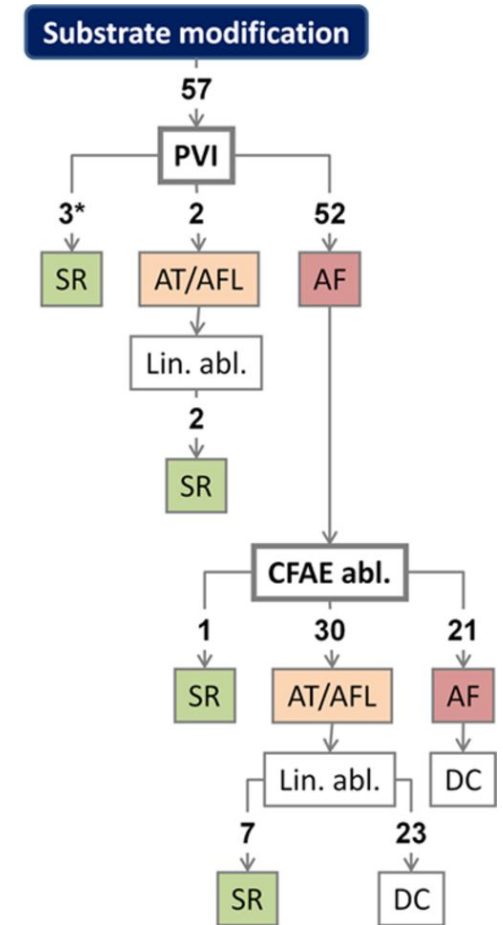
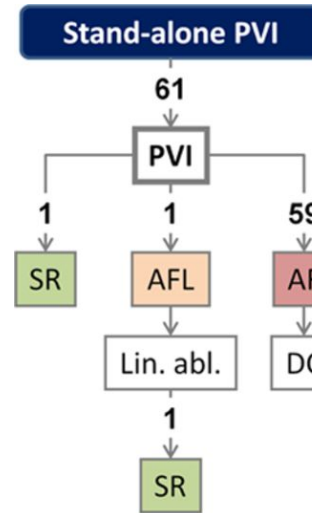
Alster-Lost-AF Trial



In patients with persistent and long-standing persistent AF, patients were randomized 1:1 to stand-alone PVI or PVI plus substrate modification -- the midterm outcomes after index ablation strategies of stand-alone PVI or a stepwise approach of PVI followed by CFAE and linear ablation.

Primary end point: Freedom from recurrence of any tachyarrhythmia (outside 12 week blanking period) of 12 months

Total 124 patients enrolled – 61 PVI only/57 PVI plus substrate modification



*n=2 in post-DC SR before PVI

Alster-Lost-AF Trial



Table 1. Baseline Patient Characteristics

Variable	All Patients, (n=118)	PVI-Only, (n=61)	Substrate Modification, (n=57)
Age, y	61.5±9.7	62.1±9.9	60.9±9.6
Female sex	34 (29)	19 (31)	15 (26)
BMI	27.9±4.0	28.1±3.8	27.8±4.2
Duration of AF, mo	12 [7, 24]	12 [7, 24]	12 [7, 24]
Type of AF			
Persistent	69 (59)	35 (57)	34 (60)
Long-standing persistent	49 (42)	26 (43)	23 (40)
CAD	11 (9)	5 (8)	6 (11)
Valvular disease	14 (12)	8 (13)	6 (11)
Hypertension	64 (54)	35 (57)	29 (51)
Diabetes mellitus	9 (8)	5 (8)	4 (7)
CHADS ₂ score	1 [0, 1]	1 [0, 1]	1 [0, 1]
0–1	103 (87)	52 (85)	51 (90)
2–3	14 (12)	8 (13)	6 (11)
>3	1 (1)	1 (2)	0 (0)
CHA ₂ DS ₂ -VASc score	2 [1, 2]	2 [1, 2]	1 [1, 2]
0–1	58 (49)	26 (43)	32 (56)
2–3	52 (44)	31 (51)	21 (37)
>3	8 (7)	4 (7)	4 (7)
LVEF ≥55%	100 (85)	50 (82)	50 (88)
LA diameter, mm	47.0±4.4	47.3±4.5	46.7±4.3

Table 2. Procedural Characteristics of Linear Ablation in the 57 Patients Randomized to Substrate Modification

	n	%
Procedures with linear ablation	32	56
Left atrial linear ablation (total)	28	49
Anterior line	13	23
Mitral isthmus line	17	30
Roof line	3	5
Posterior line	1	2
CTI block	14	25
Conversion to sinus rhythm during linear ablation	9/32	28

Table 3. Procedural Data

	PVI-Only (n=61)	Substrate Modification (n=57)	P Value
Ablation time, min	39 [31, 52]	82 [60, 99]	<0.0001
Procedure duration, min	162±56	218±53	<0.0001
Fluoroscopy time, min	19.5±8.9	23.5±8.5	0.0151
Radiation dose, cGy·cm ²	2918±2005	3976±2641	0.0162
Major complications	3 (5)	7 (12)	0.19
Cardiac tamponade	0 (0)	2 (4)	
Stroke	1 (2)	1 (2)	
Transient ischemic attack	1 (2)	0 (0)	
Groin bleeding requiring transfusion	1 (2)	2 (4)	
Groin bleeding requiring surgical therapy	0 (0)	2 (4)	
Minor complications	8 (13)	5 (9)	0.56
Minor groin complication	8 (13)	4 (7)	
Mediastinal hematoma, conservative treatment	0 (0)	1 (2)	

Alster-Lost-AF Trial

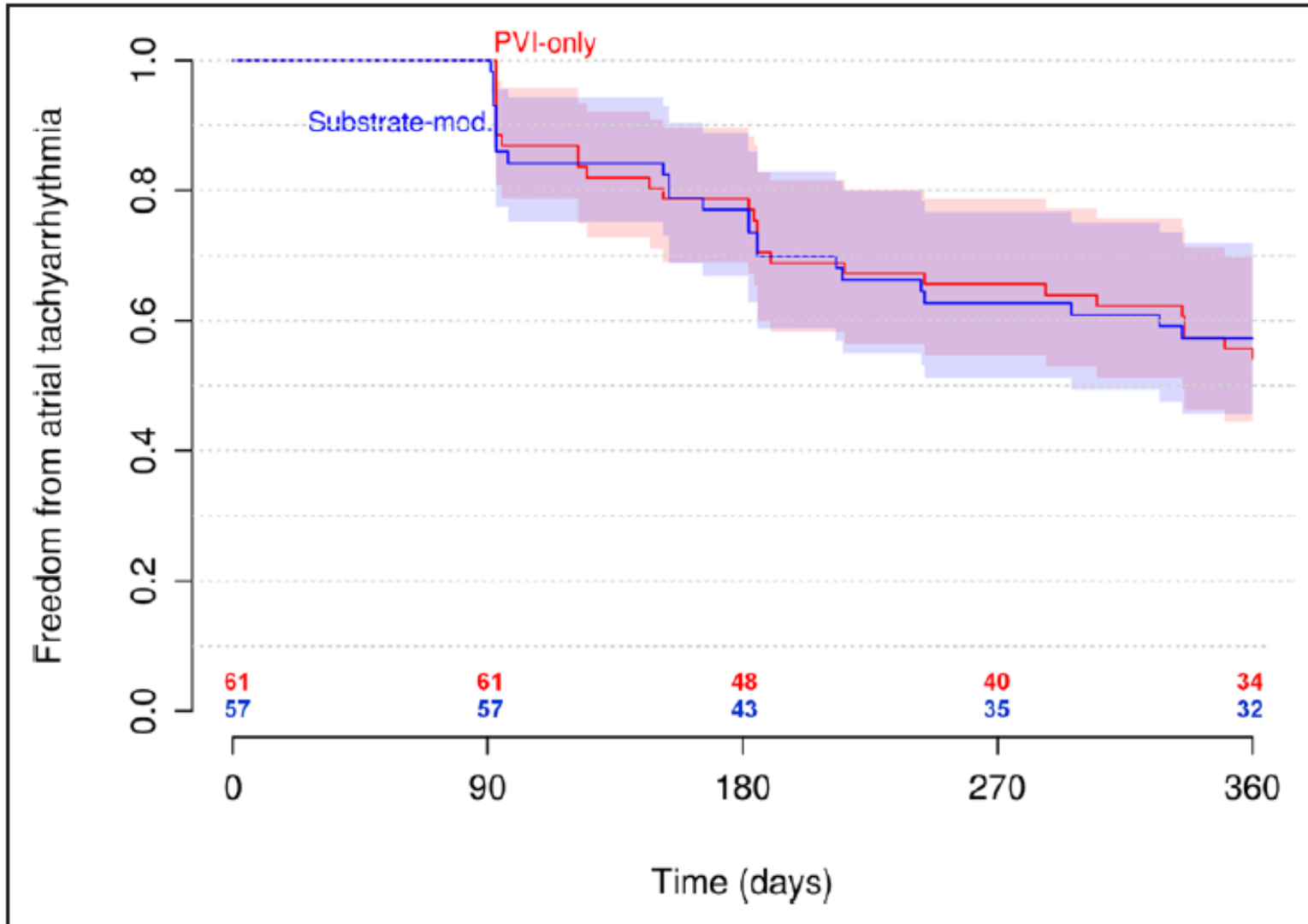


Figure 3. Freedom from recurrence of atrial tachyarrhythmias after a single procedure. One-year Kaplan–Meier estimates are 54% (95% confidence interval [CI], 43%–68%) in the pulmonary vein isolation (PVI)-only group and 57% (95% CI, 46%–72%) in the Substrate-modification group ($P=0.86$).

- The prospective and randomized Alster-Lost-AF study sought to assess, in patients with persistent and long-standing persistent AF, the midterm outcomes after index ablation strategies of stand-alone PVI or a stepwise approach of PVI followed by CFAE and linear ablation.
- No difference was observed between the 2 study arms in the primary end point of recurrence-free survival outside a 90-day blanking period at 1 year.
- It is concluded that re-conduction through gaps in the circumferential PVI lines overpowers any beneficial effect that additional substrate modification may have and that the impact of CFAE and linear ablation at the time of PVI cannot be assessed as long as durable PVI is not convincingly achieved.

Summary



- What is Mechanism of PeAF?
- Link between theory/practice/outcomes
- How do we define success?
 - Risk/Benefits of rhythm control strategy – AAD/ablation
 - Goals of therapy (reduction in AF)
 - Operator experience
 - Changes in Technology
 - Patient selection (HTN/OSA/BMI/CHADS2VASC)
- Lack RCT data to better understand risk/benefit and expectation matching (currently no ablative « cure »)

