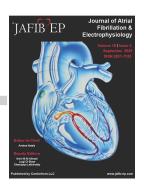


Meta-Analysis and Systematic Review

Journal of Atrial Fibrillation & Electrophysiology



www.jafib-ep.com

The addition of left atrial linear ablation to pulmonary vein isolation causes organized atrial tachycardia recurrence: a meta-analysis

Tamás János Riesz, MD¹, Róbert Pap, MD, PhD¹

¹ Cardiac Electrophysiology Division, Cardiology Center, Department of Internal Medicine, University of Szeged, Hungary

Abstract

Background: Adding left atrial linear ablation (LALA) to pulmonary vein isolation (PVI) may increase the rate of organized atrial tachycardia (OAT) recurrence. However, this association has not been formally studied. We performed a meta-analysis of studies that compared a PVI-only with a PVI + LALA strategy and reported the outcome of OAT recurrence.

Methods: A standard, random effects meta-analysis of two observational and eight randomized, controlled trials was performed. Mantel-Haenszel odds ratios (MH-OR) of pooled OAT and AF recurrence rates were calculated. Where remapping was done the pooled rate of OAT involving previous LALA-lesions was determined.

Results: Of 5536 patients, 4426 (80%) had PVI-only, 1110 (20%) had PVI + LALA. OAT occurred after PVI-only in 201 (4.5%), after PVI+LALA in 145 (13%) patients (MH-OR 2.35, 95%CI 1.40-4.07, p=0.002). Subgroup analysis pointed to increased incidence of OAT with more extensive LALA. Recurrent OAT involved previously performed LALA-lesions in 73%.

Conclusions: The performance of LALA in addition to PVI leads to an increased rate of OAT recurrence.

Correspondence:

Tamás János Riesz

Email: riesztamasj@gmail.com

Key Words

Atrial fibrillation, organized atrial tachycardia, recurrence, linear ablation

Introduction

Although no sound evidence to support it, modification of the extra-pulmonary vein (PV) atrial substrate is frequently attempted during ablation for atrial fibrillation (AF) in addition to PV isolation (PVI). A commonly adopted technique is left atrial linear ablation (LALA) including creation of a roof line connecting superior PVs and/or a mitral line either posterior or anterior to the left atrial appendage¹. Incomplete or reconnected linear lesions may create the conditions for reentry and lead to organized atrial

tachycardia (OAT) involving the gaps^{2,3}. Several studies have compared the results of AF ablation using PVI-only versus PVI + LALA and some have reported the rate of OAT recurrence as a secondary outcome. To investigate the relationship between LALA and recurrent OAT we performed a meta-analysis of studies where PVI-only and PVI + LALA strategies were compared and the outcome was reported separately for recurrent AF and OAT.

Methods

Full-text articles were selected from PubMed based on the following search string: "atrial fibrillation" and "pulmonary vein" and ablation and (linear or line) and (flutter or macroreentry or reentry) identifying 176 entries, between 1993 and June 2024. The references of selected papers were also inspected for relevant articles. Studies or subgroups of studies were included if they compared PVI-only and PVI + LALA (roof and/or mitral lines) approaches. Subgroups or studies were excluded if substrate

modification other than LALA was performed in more than 10% of the patients. These techniques included left atrial posterior wall (box-) isolation, excluded due to the heterogeneous lesion sets used in studies and the frequent employment of focal ablations on the posterior wall. Furthermore, strategies based on electrogram-based or low-voltage zone ablation were excluded. We also excluded studies where the number of patients with recurrence of OAT was not specified.

Mantel–Haenszel odds ratios (MH-OR) with 95% confidence intervals (CI) were calculated for pooled OAT and AF recurrence rates in a standard random-effect meta-analysis. From studies where mapping of recurrent OAT was performed, the pooled rate of iatrogenic arrhythmia (i.e. OAT involving previous LALA) was calculated. The I² test was used to determine the degree of heterogeneity across the studies. Subgroup analyses were conducted to explore the source of heterogeneity. Analyses were performed using Comprehensive Meta-Analysis v3.3.070 (Biostat, Inc., USA).

Results

From 176 papers, two single-centre, observational studies^{4,5}, and eight randomized, controlled trials (RCT)⁶⁻¹³ met the inclusion criteria (**Table 1**). Only paroxysmal AF patients were included in three, while only persistent AF in two studies. The rest included both paroxysmal and persistent AF patients in different ratios. Regarding the LALA performed: only roof line was created in 2 studies, only mitral line in one, while both lines were performed in the remaining seven studies. Radiofrequency ablation was utilized in all studies.

Out of the total 5536 patients, 4426 (80%) had PVI-only, while 1110 (20%) had PVI + LALA. After PVI-only 201 (4.5%) patients experienced recurrence of OAT, while after PVI + LALA recurrence of OAT occurred in 145 (13%). Seven studies reported the AF recurrence rates also, among the same patients. The pooled rates of AF recurrence in these studies after PVI-only and PVI + LALA were 41% and 38%, respectively.

The meta-analysis confirmed a significantly higher rate of OAT recurrence after PVI + LALA, compared to PVI-only (MH-OR 2.35, 95%CI 1.40-4.07, p=0.002) (**Figure 1**.). To explore the source of considerable heterogeneity (I²=60%), a subgroup analysis was performed comparing studies in which only one (roof or mitral) line was created to those where both LALA were performed. In the three studies utilizing a single LALA there was no significant effect size in terms of OAT recurrence (MH-OR 1.43, 95%CI 0.39-5.23, p=0.590). The combination of the remaining seven studies where both lines were created showed a significantly higher rate of OAT recurrence with LALA (MH-OR 2.80, 95%CI 1.43-5.49, p=0.003). There was no significant difference in the pooled rate of AF recurrence after PVI + LALA and PVI-only strategies (MH-OR 0.59, 95%CI 0.28-1.21, p=0.146) (**Figure 2**.).

Four studies reported the results of mapping of recurrent OAT during a redo procedure. The pooled frequency of the arrhythmia being related to gaps in previous LALA was 44/60 (73%).

Figure: 1

Forest plot of odds ratios (PVI + LALA / PVI-only) for organized atrial tachycardia recurrence

Study name							MH	odo	is ra	itio	and	95% (CI
	PVI + LALA	PVI-only	Relative I weight		p-Value								
Fassini 2005	3 / 95	0/92	2,98	7,000	0,200			-	+	+	+	+	-
Willems 2006	2/32	1 / 30	4,13	1,933	0,599		+		+	+	•	_	\rightarrow
Gaita 2008	13 / 121	4/62	11,35	1,745	0,349				-	+	-	-	
Sawhney 2010	8 / 33	0/33	3,12	22,333	0,036					-	+	-	-
Mun 2012	4 / 52	2/52	6,96	2,083	0,409			-	+	+	•	_	-
Arbelo 2014	3 / 59	5/61	8,66	0,600	0,498		+	_	-	+	+		
Verma 2015	34 / 244	7 / 61	14,68	1,249	0,615				-	+	+	-	
Wynn 2016	7 / 63	2/61	7,74	3,688	0,113					+	_	•	-
pek 2019	31 / 119	74 / 485	19,66	1,957	0,006					-		-	
im 2024	40 / 292	106 / 3489	20,74	5,066	0,000							-	-
Pooled .				2,349	0,002						•	▶	
						0,1	0,2	2	0,5	1	2	5	1
						F	avour	s PV	I+LAI	.A	Favo	urs PVI	

Figure: 2

Forest plot of odds ratios (PVI + LALA / PVI-only) for atrial fibrillation recurrence

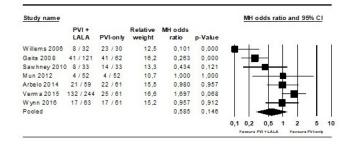


Table: 1

Characteristics of included studies

Study	Design	AF type	LALA	Follow-up (months)	latrogenic OAT (mapped)	Other OAT (mapped)
Fassini 2005	RCT (single centre)	67% paroxysmal, 33% persistent	mitral line (posterior)	> 12		
Willems 2006	RCT (single centre)	100% persistent	roof line, mitral line (posterior)	16 (median)	2/2 - both perimitral with incomplete line	
Gaita 2008	RCT (single centre)	61% paroxysmal, 39% persistent	roof line, mitral line (posterior)	>36	7/13 - 6 perimitral, 1 roof-dependent	RA macroreentry, LA microreentry
Sawhney 2010	RCT (single centre)	100% paroxysmal	roof line, mitral line (posterior)	16 (mean)	6/9 - 4 perimitral, 2 roof dependent	LA ridge related
Mun 2012	RCT (single centre)	100% paroxysmal	roof line, mitral line (posterior)	16 (mean)		
Arbelo 2014	RCT (single centre)	100% paroxysmal	roof line	16 (mean)		
Verma 2015	RCT (single centre)	100% persistent	roof line, mitral line (posterior)	18		
Wynn 2016	RCT (single centre)	61% persistent, 39% sustained paroxysmal	roof line, mitral line (posterior)	12		
lpek 2019	observational	59% paroxysmal, 41% persistent	roof line, CFAE (5%)	28 (median)		
Lim 2024	observational	both (% not reported)	roof line, mitral line (anterior or posterior), CFAE (8.6%)	77 (mean)	29/36 - 25 perimitral, 7 roof-dependent	LA anterior, septal

Table: Characteristics of included studies. RCT=randomized controlled trial, AF=atrial fibrillation, LALA=left atrial linear ablation, CFAE=complex fractionated atrial electrogram, OAT=organized atrial tachycardia, RA=right atrial, LA=left atrial.

Discussion

This meta-analysis of available studies showed an increased rate of OAT recurrence after adjunctive linear ablation on top of PVI in the treatment of AF. This association was most pronounced in case of studies employing a more extensive LALA lesion set. The increased rate of OAT recurrence was not offset by less AF recurrence after LALA in this meta-analysis. Furthermore, the OAT observed after LALA was related to gaps in the previously performed ablation line in more than 70% of the cases.

Empirical LALA is still employed in a considerable proportion of cases, despite the fact that it has not been shown to improve the outcome of AF ablation and it is not recommended by the latest guideline¹. In addition to its limited effectiveness on top of PVI, LALA by contemporary RF technology leads to an increased rate of OAT recurrence. This proarrhythmic effect is probably related to incompleteness and low durability of linear lesions produced by legacy techniques. Slow conduction through gaps in the lines provides the requirement for the development of macroreentry^{2,3}. New catheter design or energy source (e.g. pulsed electric field) may result in more durable LALA and less OAT recurrence in the future.

Conclusion

The findings of this meta-analysis question the utility of performing LALA in addition to PVI and point to the iatrogenic nature of OAT recurrence after linear ablation.

Statements and Declarations

- Data available on reasonable request from the corresponding author.
- Funding and conflict of interest: No conflict of interest can be disclosed on behalf of the authors. The authors did not receive support from any organization for the submitted work.
- As a meta-analysis, informed consent was taken from the patients by the authors of the included studies. Animal studies were not involved in the analysis.
- Our work does not have a clinical trial registration.
- No materials were reproduced from other sources, hence no permission was necessary.

References

- 1. Tzeis S, Gerstenfeld EP, Kalman J et al. 2024 European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Europace*. 2024 Mar 30;26(4):euae043. doi: 10.1093/europace/euae043
- 2. Kitamura T, Takigawa M, Derval N, et al. Atrial tachycardia circuits include low voltage area from index atrial fibrillation ablation relationship between RF ablation lesion and AT. *J Cardiovasc Electrophysiol*. 2020;31(7):1640-1648. doi:10.1111/jce.14576
- 3. Takagi T, Derval N, Duchateau J et al. Gaps after linear ablation of persistent atrial fibrillation (Marshall-PLAN): Clinical implication. *Heart Rhythm*. 2023 Jan;20(1):14-21. doi: 10.1016/j.hrthm.2022.09.009
- Ipek EG, Marine J, Yang E, Habibi M, Chrispin J, Spragg D, Berger RD, Calkins H, Nazarian S. Predictors and Incidence of Atrial Flutter After Catheter Ablation of Atrial Fibrillation. *Am J Cardiol*. 2019 Dec 1;124(11):1690-1696. doi:10.1016/j.amjcard.2019.08.026. Epub 2019 Sep 6. PMID: 31607374.
- Lim MW, Morton M, Fernando R, Elbracht-Leong S, Better N, Segan L, William J, Crowley R, Morton JB, Sparks PB, Lee G, McLellan AJ, Ling LH, Sugumar H, Prabhu S, Voskoboinik A, Kalman JM, Kistler PM. Impact of Posterior Wall Isolation During AF Ablation on the Incidence of Left Atrial Flutter. *JACC Clin Electrophysiol*. 2024 May 9:S2405-500X(24)00286-X. doi: 10.1016/j.jacep.2024.04.008. Epub ahead of print. PMID: 38752960.
- Fassini G, Riva S, Chiodelli R, Trevisi N, Berti M, Carbucicchio C, Maccabelli G, Giraldi F, Bella PD. Left mitral isthmus ablation associated with PV Isolation: long-term results of a prospective randomized study. *J Cardiovasc Electrophysiol.* 2005 Nov;16(11):1150-6. doi: 10.1111/j.1540-8167.2005.50192.x. PMID: 16302895.
- 7. Willems S, Klemm H, Rostock T, Brandstrup B, Ventura R, Steven D, Risius T, Lutomsky B, Meinertz T. Substrate modification combined with pulmonary vein isolation improves outcome of catheter ablation in patients with persistent atrial fibrillation: a prospective randomized comparison. *Eur Heart J.* 2006 Dec;27(23):2871-8. doi: 10.1093/eurheartj/ehl093. Epub 2006 Jun 16. PMID: 16782716.
- Gaita F, Caponi D, Scaglione M, Montefusco A, Corleto A, Di Monte F, Coin D, Di Donna P, Giustetto C. Long-term clinical results of 2 different ablation strategies in patients with paroxysmal and persistent atrial fibrillation. Circ Arrhythm Electrophysiol. 2008 Oct;1(4):269-75. doi: 10.1161/CIRCEP.108.774885. PMID: 19808418.
- Sawhney N, Anousheh R, Chen W, Feld GK. Circumferential pulmonary vein ablation with additional

- linear ablation results in an increased incidence of left atrial flutter compared with segmental pulmonary vein isolation as an initial approach to ablation of paroxysmal atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2010 Jun;3(3):243-8. doi: 10.1161/CIRCEP.109.924878. Epub 2010 Mar 25. PMID: 20339034.
- Mun HS, Joung B, Shim J, Hwang HJ, Kim JY, Lee MH, Pak HN. Does additional linear ablation after circumferential pulmonary vein isolation improve clinical outcome in patients with paroxysmal atrial fibrillation? Prospective randomised study. *Heart*. 2012 Mar;98(6):480-4. doi: 10.1136/heartjnl-2011-301107. Epub 2012 Jan 27. PMID: 22285969; PMCID: PMC3285139.
- Arbelo E, Guiu E, Ramos P, Bisbal F, Borras R, Andreu D, Tolosana JM, Berruezo A, Brugada J, Mont L. Benefit of left atrial roof linear ablation in paroxysmal atrial fibrillation: a prospective, randomized study. *J Am Heart Assoc.* 2014 Sep 5;3(5):e000877. doi: 10.1161/JAHA.114.000877. PMID: 25193295; PMCID: PMC4323787.
- 12. Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, Albenque JP, Nardi S, Menardi E, Novak P, Sanders P; STAR AF II Investigators. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med. 2015 May 7;372(19):1812-22. doi: 10.1056/NEJMoa1408288. PMID: 25946280.
- 13. Wynn GJ, Panikker S, Morgan M, Hall M, Waktare J, Markides V, Hussain W, Salukhe T, Modi S, Jarman J, Jones DG, Snowdon R, Todd D, Wong T, Gupta D. Biatrial linear ablation in sustained nonpermanent AF: Results of the substrate modification with ablation and antiarrhythmic drugs in nonpermanent atrial fibrillation (SMAN-PAF) trial. *Heart Rhythm*. 2016 Feb;13(2):399-406. doi: 10.1016/j.hrthm.2015.10.006. Epub 2015 Oct 9. PMID: 26455343.