Low-Voltage Myocardium-Guided Ablation Trial of Persistent Atrial Fibrillation (ERASE-AF) Trial

Huo, Y. et al. (2022). NEJM Evid, 1(11):EVIDoa2200141.

Introduction

Yan Huo (Dresden Heart Center, Dresden, Germany) and colleagues report on whether pulmonary vein isolation (PVI) with or without individual substrate modification (SM) at targeted low-voltage atrial tissue improves freedom from atrial arrhythmia (AA) recurrence in persistent and long-standing persistent atrial fibrillation (LSPAF) in the ERASE AF Trial.[1]

Methods

ERASE-AF is a multicenter, randomized, superiority, parallel-group, open-label trial with blinded endpoint assessment which enrolled 324 patients in Europe between April 2016 and October 2019. All patients with persistent or LSPAF who did not have prior left atrial (LA) ablation were randomized one-to-one to undergo either PVI alone or PVI+SM endocardial catheter ablation. The primary efficacy endpoint was time to first recurrence of AF or atrial tachycardia (AT) ≥ 30 sec after a three-month blanking period after a single ablation procedure.

Endocardial mapping was conducted using commercial methods. Patients in the PVI-only group underwent PVI such that diseased arrhythmogenic atrial regions, including the posterior LA wall, remained untouched. Conversely, patients in the PVI+SM group received ablations to the pulmonary veins (PVs) and low-voltage atrial tissue. Examples of low-voltage guided substrate modification included: right anterior PV antrum areas close to the mitral annulus, right and left inferior and superior PV, LA septum, entire posterior and anterior LA wall and right and left posterior PV antrum. Patients in the PVI+SM group who received a PVI-only ablation were analyzed as intent-to-treat.

Post-ablation, class I/III antiarrhythmic drugs (AAD) were discontinued but restarted at physician's discretion in instances of AA recurrence. Documentation of AAD use occurred in both treatment arms. Repeat ablations could also be performed after the 90-day blanking period as needed. Arrhythmia recurrence prior to reaching the primary endpoint requiring re-ablation was considered a therapy failure.

All patients underwent seven-day serial electrocardiogram (ECG) recordings at three-, six- and 12-months post-procedure. Any documented AA data from any clinical, wearable, implanted ECG device also contributed equally to the primary endpoint. Continuous monitoring data was obtained from patients with implantable cardiac monitoring (ICM) devices.

Results

After randomization one-to-one, 163 received PVI and 161 received PVI+SM. Both groups had similar baseline characteristics. At baseline, 93% of patients had persistent AF and 7% had LSPAF, mean LA size was 4.5 cm, and ejection fraction was normal (mean of 53%). Time of AF history was 31 (11-77 months). Low-voltage areas were identified in 36% (118/324) of the patient population; 53% (63/118) of these patients had low-voltage areas in the LA posterior wall.

In this intent-to-treat analysis, significantly fewer patients in the PVI+SM arm experienced AF/AT recurrence as compared to those who underwent PVI alone (35% vs 50%, P=0.010). Similarly, lower AF/AT recurrence rates were observed among PVI+SM patients with ICMs (35% vs 55%). Post-operatively, rates of AAD continuation and repeat catheter ablation were similar between arms (Table). Oral anticoagulation status during follow-up was not reported.

Efficacy Outcomes			
	PVI+SM	PVI Only	P-Value
Freedom from AF/AT recurrence, % (n/N)	35% (54/153)	50% (75/150)	0.010
Freedom from AF/AT recurrence in patients with ICM, % (n/N)	39% (47/120)	55% (65/119)	NS
Post-operative antiarrhythmic drugs, % (n)	11% (17)	13% (19)	NS
Repeat ablation, % (n)	3% (4)	9% (13)	NS

AF/AT=atrial fibrillation/atrial tachycardia; ICM=implantable cardiac monitor; PVI+SM=pulmonary vein isolation + substrate modification

Adverse event rates trended higher (3.7%, 6/161 vs 1.8%, 3/163) among patients in the PVI+SM group compared to PVI alone, respectively. Most common adverse events were arteriovenous fistula, pseudoaneurysm at vascular access sites (10 total). Post-procedural cardiac tamponade occurred in two patients in the PVI+SM group. The first and second patients were treated with pericardial puncture and drainage of 350 ml and 270 ml of blood, respectively. No cardiac surgery was needed in either case and both made a full recovery. No stroke, phrenic nerve injury, atrioesophageal fistula, PV stenosis or deaths were observed in the trial.

Subgroup Analyses

Patients without identified areas of low-voltage myocardium and who only underwent PVI had the lowest risk of AF recurrence regardless of treatment assignment. Conversely, patients with identified areas of low-voltage myocardium who received only PVI had the highest risk of AF recurrence (63%). Among 24 patients with LSPAF, PVI-only treated patients were nearly three times more likely to experience AF/AT recurrence (77% vs 27%).

Key Takeaways

- In this endocardial catheter ablation trial, persistent and LSPAF patients who underwent PVI+SM experienced greater freedom from AF/AT through 12 months as compared to those who underwent PVI alone.
- Untreated areas of the left atria were the primary culprits of AF/AT recurrence. In addition, epicardial gaps and substrates that are either unrecognized and/or untreated can also become arrhythmogenic.
- Even with sophisticated mapping of low voltage myocardium and selective lesion creation in the PVI+SM group, AF/AT recurrence was still possible.

References:
1. *Huo, Y. et al. (2022). NEJM Evid, 1(11):EVIDoa2200141.*

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