

# **New Evidences on Substrate Modification in Persistent Atrial Fibrillation**

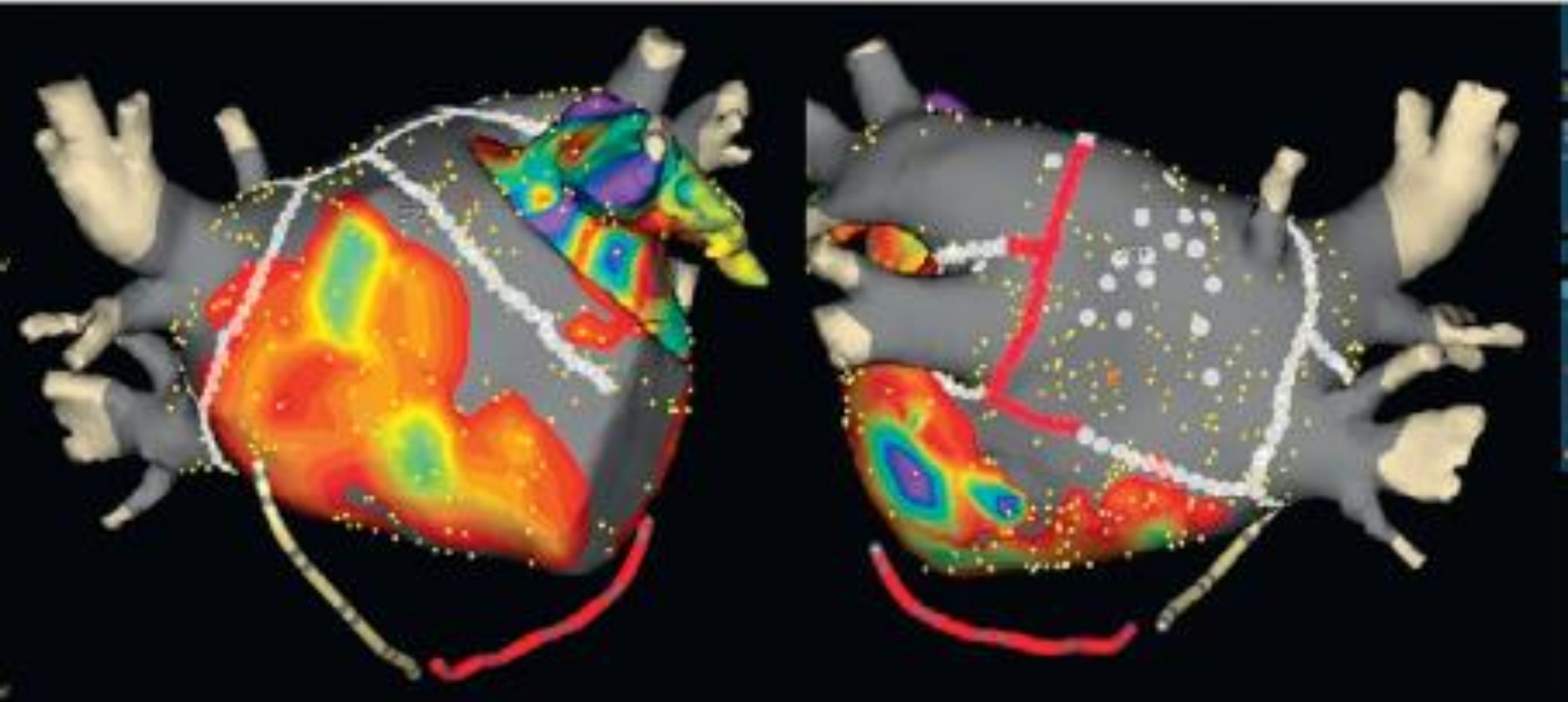
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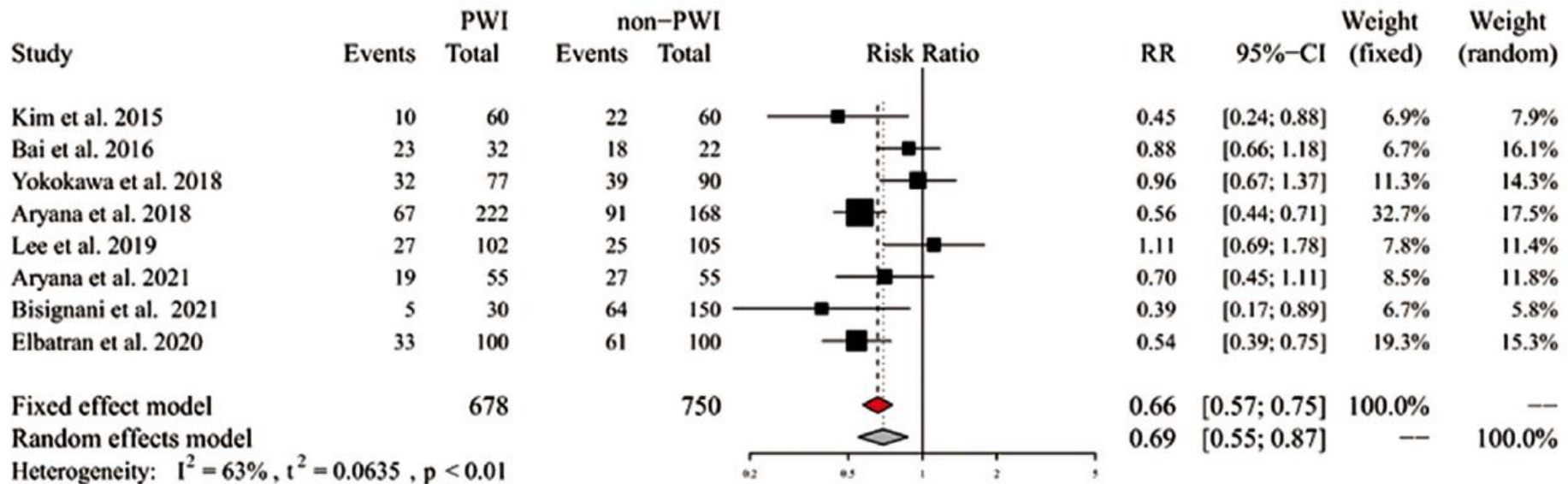
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- Posterior wall isolation
- Low-voltage myocardium-guided ablation
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# Posterior Wall Isolation

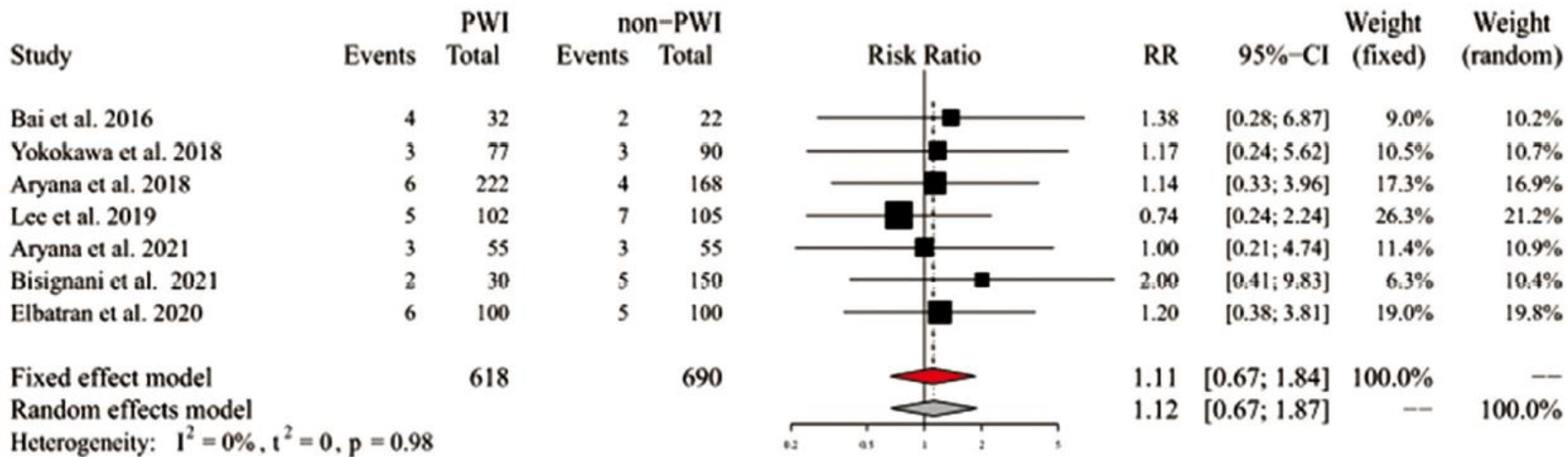


# Efficacy of Posterior Wall Isolation



**FIGURE 2** Forest plot of pooled result for atrial arrhythmia recurrence comparing PWI with non-PWI in catheter ablation for persistent atrial fibrillation. PWI, posterior wall isolation [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

# Safety of Posterior Wall Isolation



**FIGURE 3** Forest plot of pooled result for procedural adverse events comparing PWI with non-PWI in catheter ablation for persistent atrial fibrillation. PWI, posterior wall isolation [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

# Post Wall Isolation; Subgroup Analysis

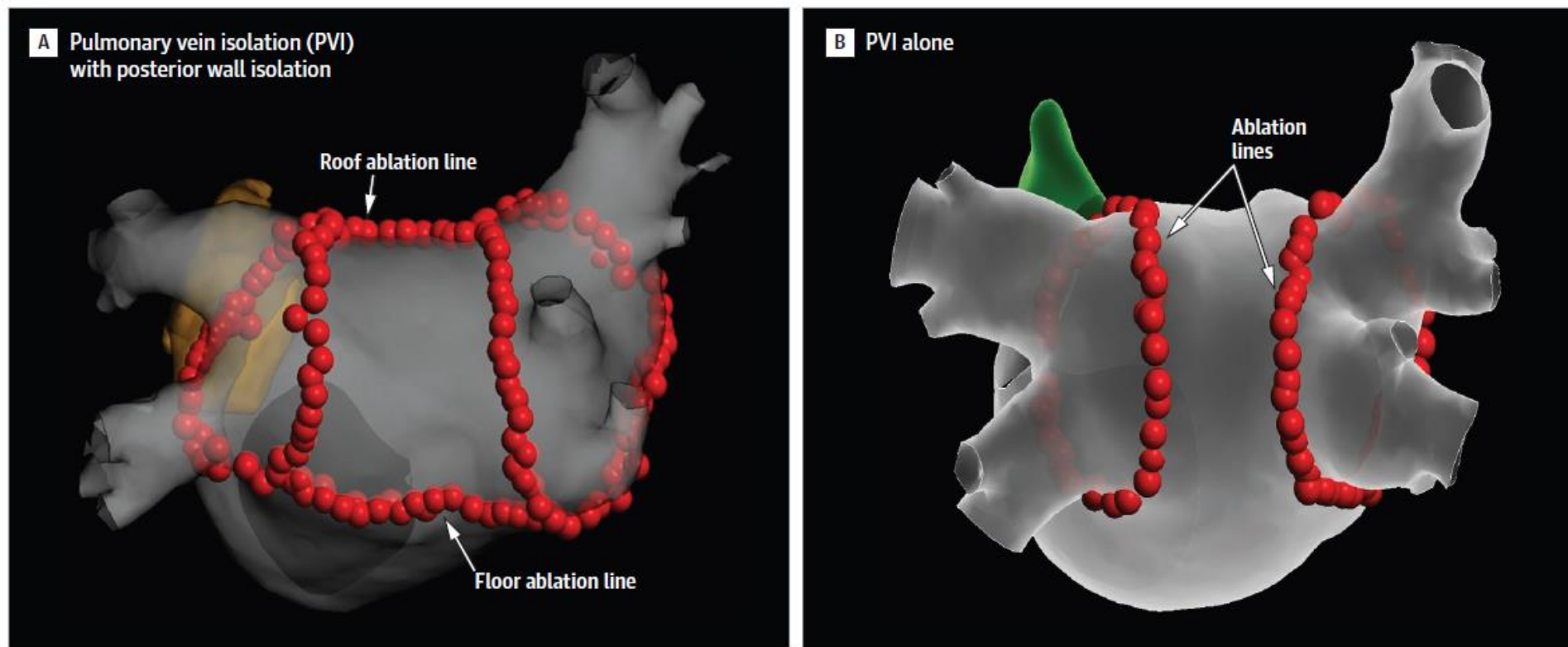
## 1. AA recurrence

### AA type

AF recurrence	8	147/678	277/750		0.57(0.40~0.80)	70%
AT recurrence	7	66/618	69/690		0.92(0.67~1.27)	42%
<b>Study design</b>						
RCT+PSM	5	94/347	199/470		0.63(0.45~0.88)	55%
Non-RCT	3	112/331	148/280		0.77(0.54~1.10)	77%
<b>Ablation energy</b>						
CBA	3	91/307	143/283		0.57(0.46~0.70)	0%
RFA	4	93/294	126/287		0.72(0.49~1.05)	71%
<b>PWI mode</b>						
Endocardial box isolation	3	69/239	86/255		0.84(0.54~1.30)	61%
Debulking ablation	4	114/339	200/395		0.65(0.47~0.90)	64%

# Posterior Wall Isolation; CAPLA Trial

Figure 1. Pulmonary Vein Isolation With and Without Posterior Wall Isolation



A, Pulmonary vein isolation (PVI) with posterior wall isolation achieved by adding a roof ablation line connecting the superior aspects of the pulmonary veins and floor

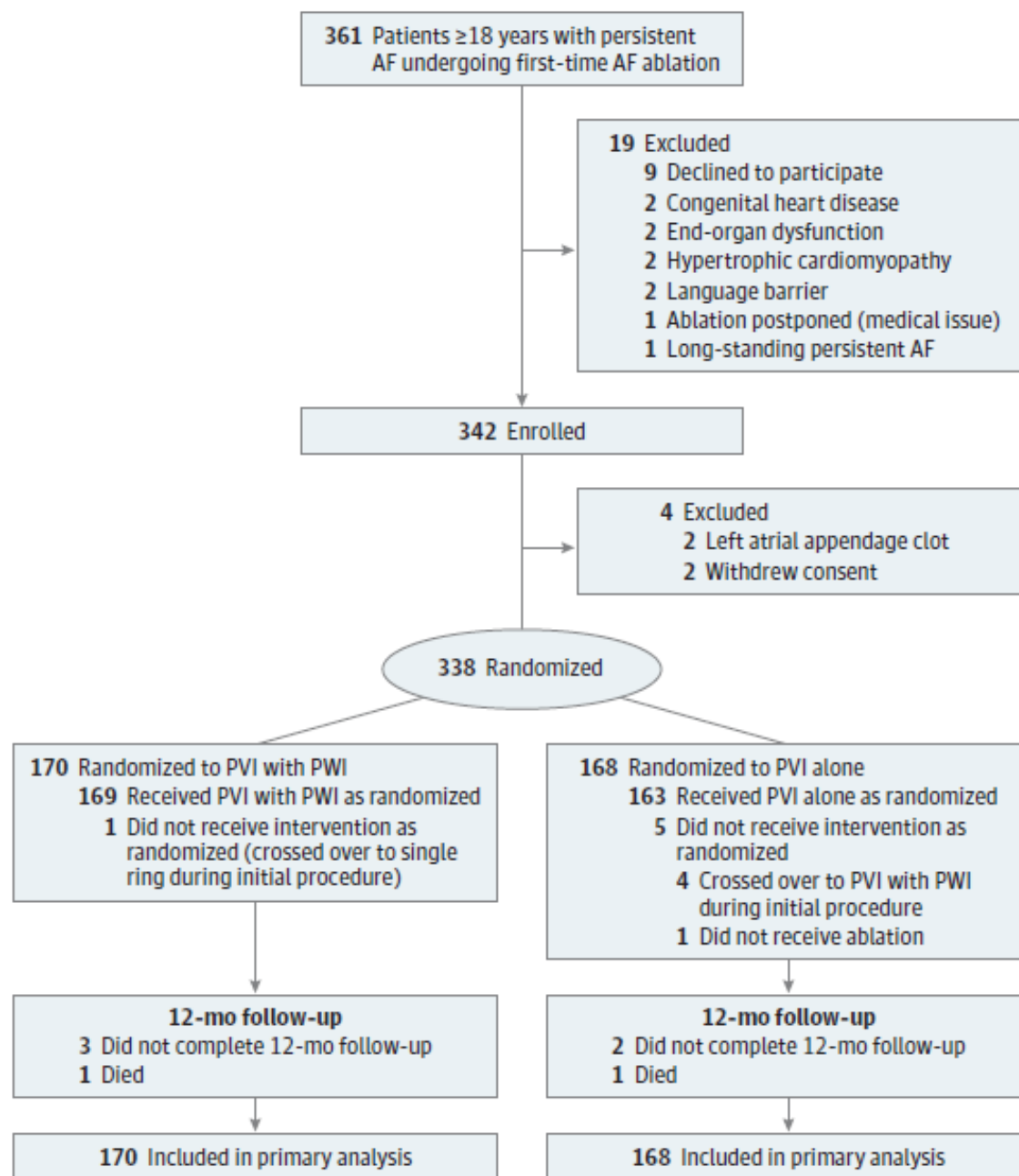
ablation line connecting the inferior aspects of the pulmonary veins. B, Wide antral circumferential ablation around the pulmonary veins bilaterally to achieve PVI.

**Table 1. Cohort Characteristics**

Characteristic	No. (%)	
	PVI + PWI (n = 170)	PVI alone (n = 168)
<b>Demographics</b>		
Age, median (IQR), y	65.7 (58.7-71.1)	65.5 (57.8-71.7)
Men	131 (77.1)	128 (76.2)
Women	39 (22.9)	40 (23.8)
BMI, median (IQR) <sup>a</sup>	29.1 (26.3-32.8)	28.6 (26.0-33.1)
Longest median continuous duration of AF, median (IQR), mo	5 (2-8)	5 (2-8)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score, median (IQR) <sup>b</sup>	2 (1-3)	2 (1-3)
No. of cardioversions before ablation, median (IQR)	2 (1-2)	2 (1-2)
<b>Comorbidities</b>		
Obesity (BMI >27 <sup>a</sup> )	110 (64.7)	110 (65.5)
Hypertension	85 (50.0)	74 (44.0)
Congestive cardiac failure <sup>c</sup>	45 (26.5)	53 (31.5)
Ischemic heart disease	18 (10.6)	23 (13.7)
Type 2 diabetes	17 (10.0)	18 (10.7)
Stroke	11 (6.5)	7 (4.2)
<b>No. of failed antiarrhythmic medications</b>		
0	14 (8.2)	17 (10.1)
1	117 (68.8)	117 (69.6)



Figure 2. Recruitment, Randomization, and Patient Flow in the CAPLA Trial



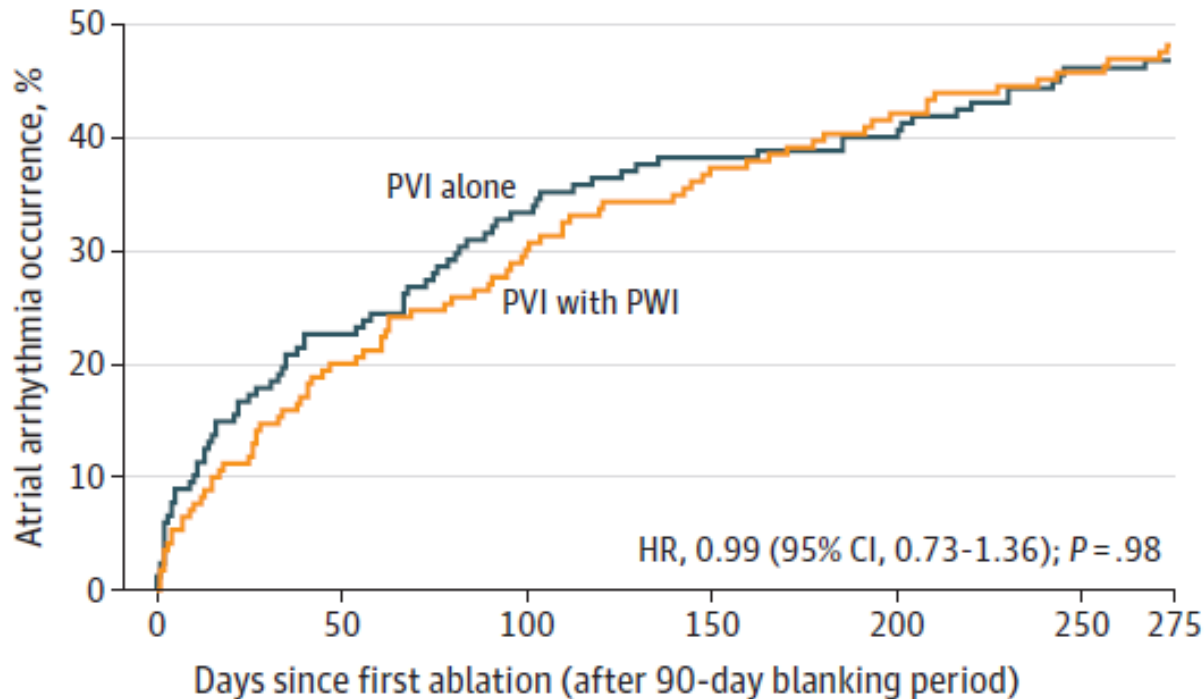
# Posterior Wall Isolation; CAPLA Trial

Table 2. Major Efficacy Outcomes

	No. (%)			P value
	PVI + PWI (n = 170)	PVI alone (n = 168)	Absolute difference	
<b>Primary outcome</b>				
Freedom from any documented atrial arrhythmia, after a single ablation procedure, without antiarrhythmic medications	89 (52.4)	90 (53.6)	-1 (-1.2)	.98
<b>Secondary outcomes</b>				
Freedom from any documented atrial arrhythmia episodes >30 s at 12 mo after 1 or 2 ablation procedures with or without antiarrhythmic medications	99 (58.2)	101 (60.1)	-2 (-1.9)	.57
Freedom from documented atrial flutter or atrial tachycardia episodes >30 s at 12 mo after 1 or 2 ablation procedures with or without antiarrhythmic medications	142 (84.5)	148 (87.1)	-6 (-2.6)	.31
Freedom from symptomatic AF episodes >30 s at 12 mo after 1 or 2 ablation procedures with or without antiarrhythmic medications	116 (68.2)	121 (72.0)	-5 (-3.8)	.36
Freedom from symptomatic atrial arrhythmia episodes >30 s at 12 mo after 1 or 2 ablation procedures with or without antiarrhythmic medications	114 (67.0)	119 (70.8)	-5 (-3.8)	.45

# Posterior Wall Isolation; CAPLA Trial

Figure 3. Any Atrial Arrhythmia Recurrence, Without Antiarrhythmic Medication, After a Single Ablation Procedure



Cumulative No.  
of events

PVI alone	0	46	61	65	72	78	78
PVI with PWI	0	42	58	66	74	81	81

# Conclusion; Posterior Wall Isolation

- In patients with persistent AF, the addition of posterior wall isolation to pulmonary vein isolation did not significantly improve freedom from atrial arrhythmia compared with pulmonary vein isolation alone.

# Low-Voltage Myocardium-Guided Ablation: ERASE-AF Trial

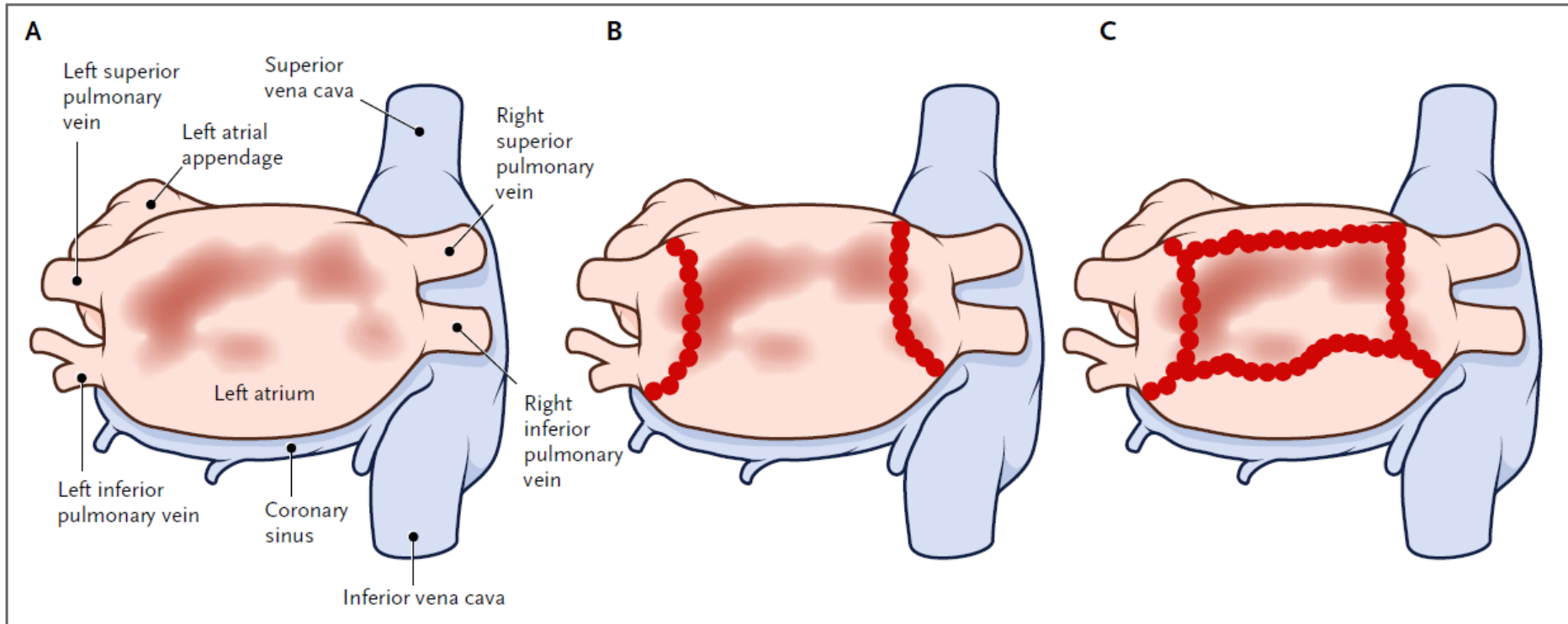


Figure 1. Concept of Low-Voltage Myocardium-Guided AF Substrate Ablation.

Panel A is an example of a view at the posterior left atrial wall, where voltage mapping has identified extended areas of atrial low-voltage myocardium outside of the ostia of the pulmonary veins. (Panel B) An ablation approach that would only target the pulmonary veins (pulmonary vein isolation [PVI] only group) is displayed here. The diseased arrhythmogenic atrial tissue at the posterior left atrial wall would be left untreated. This tissue could continue to cause recurrences of atrial fibrillation (AF) and atrial tachycardia. (Panel C) Individualized ablation of atrial low-voltage myocardium (PVI plus substrate modification [PVI+SM] group) specifically targets such additional diseased arrhythmogenic tissue on top of PVI. The ERASE-AF (Low-Voltage Myocardium-Guided Ablation Trial of Persistent Atrial Fibrillation) trial investigated whether the ablation of these additional arrhythmia sources improves freedom from arrhythmia recurrences.

**Table 1. Baseline Characteristics.\***

<b>Characteristic</b>	<b>Total (N=324)</b>	<b>PVI+SM (n=161)</b>	<b>PVI Only (n=163)</b>
Age — yr	66±10	65±10	66±10
Gender — male	216 (67)	112 (70)	104 (64)
AF history — mo	31 (11–77)	31 (8–77)	31 (12–77)
Longstanding persistent AF	24 (7)	11 (7)	13 (8)
BMI	30±5	29±5	30±5
HTN	267 (82)	130 (81)	137 (84)
DM	80 (25)	40 (25)	40 (25)
CHF	74 (23)	32 (20)	42 (26)
PAD	21 (6)	8 (5)	13 (8)
CAD	94 (29)	48 (30)	46 (28)
Previous TIA/stroke	27 (8)	12 (7)	15 (9)
EHRA score	2 (2–3)	2 (2–3)	2 (2–3)
CHA2DS2-VASc	3 (2–4)	3 (2–4)	3 (2–4)
pfAA	316 (98)	158 (98)	158 (97)
OAC	315 (97)	155 (96)	160 (98)
LVEF — %	53±11	53±12	54±11
LAD — mm	45±7	45±7	45±6

# Low-Voltage Myocardium-Guided Ablation: ERASE-AF Trial

**Table 2. Intention-to-Treat, Efficacy End Points.\***

Outcome After Index Procedure	PVI Only†	PVI+SM†	Percent Difference (95% CI)‡
Efficacy end point			
Primary (n=303)	75/150 (50)	54/153 (35)	15 (4 to 26)
Secondary (n=239)	65/119 (55)	47/120 (39)	15 (3 to 28)
Antiarrhythmic drugs§	19/150 (13)	17/153 (11)	2 (-6 to 9)
Reablation	13/150 (9)	4/153 (3)	6 (1 to 11)

# Low-Voltage Myocardium-Guided Ablation: ERASE-AF Trial

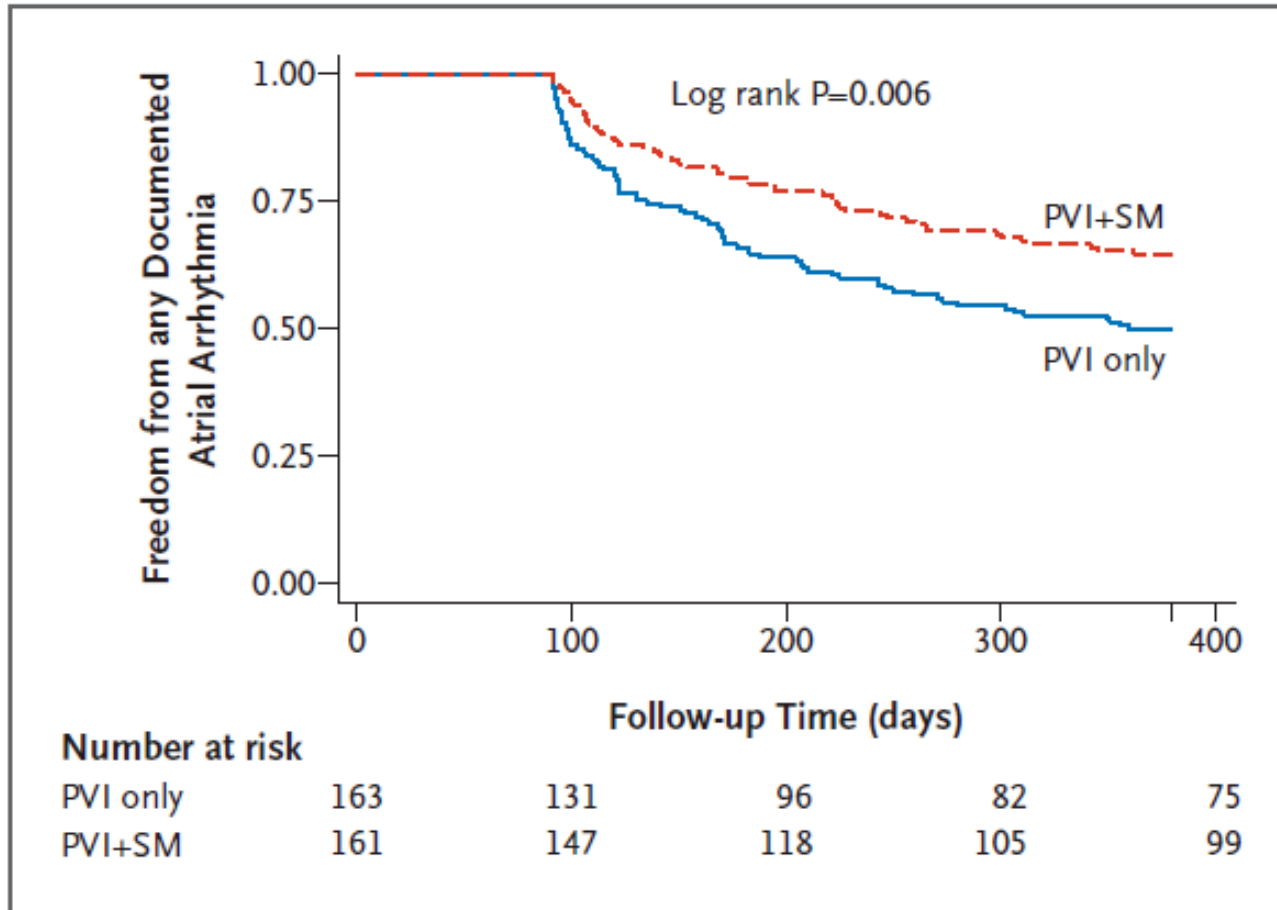


Figure 2. Intention-to-Treat, Primary Efficacy End Point.



# Conclusion; Low-Voltage Myocardium-Guided Ablation

- In patients with persistent AF, pulmonary vein isolation plus individualized ablation of atrial low-voltage myocardium significantly improved outcomes.

# MRI-Guided Fibrosis Ablation; DECAAF II Trial

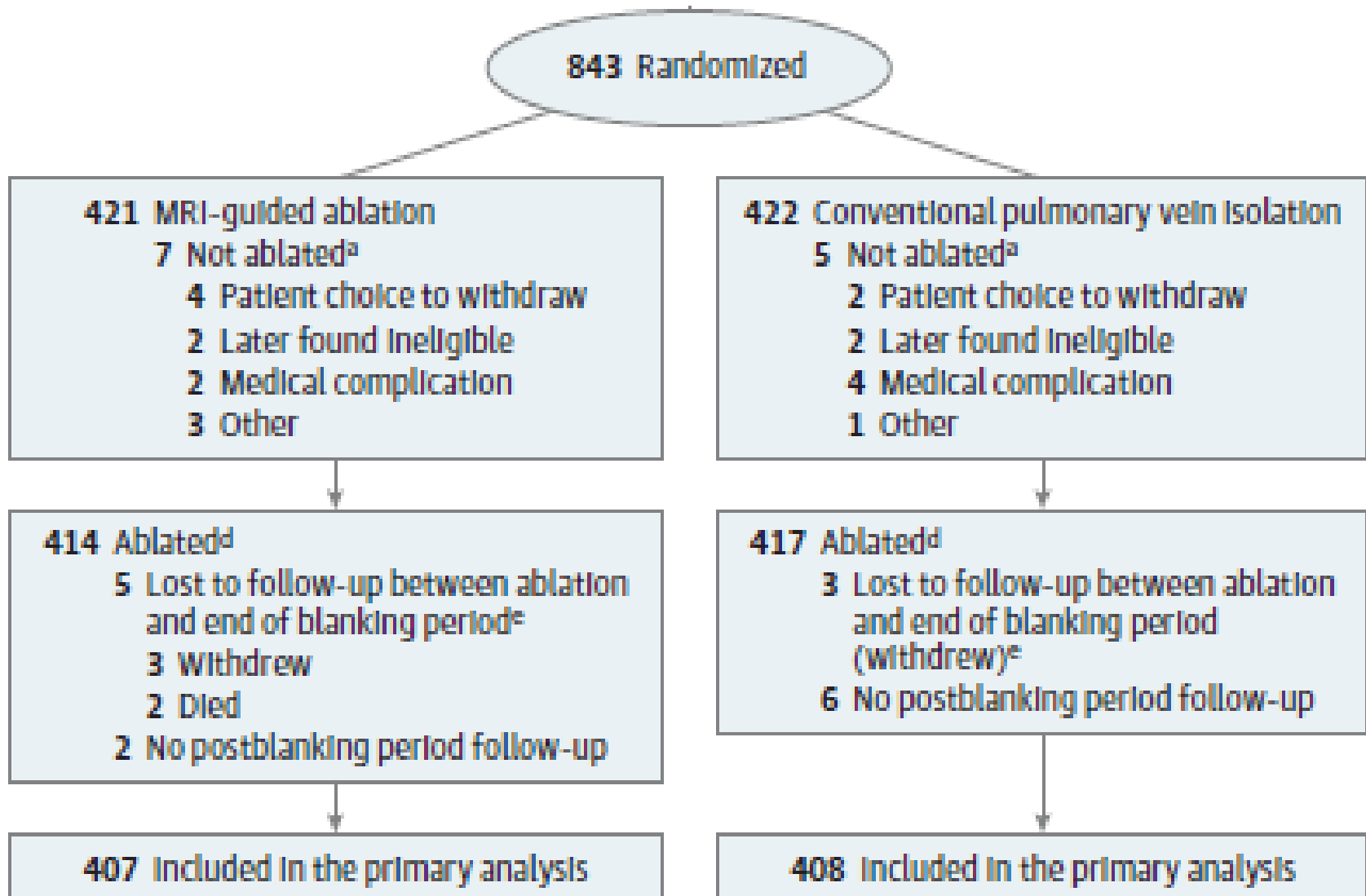
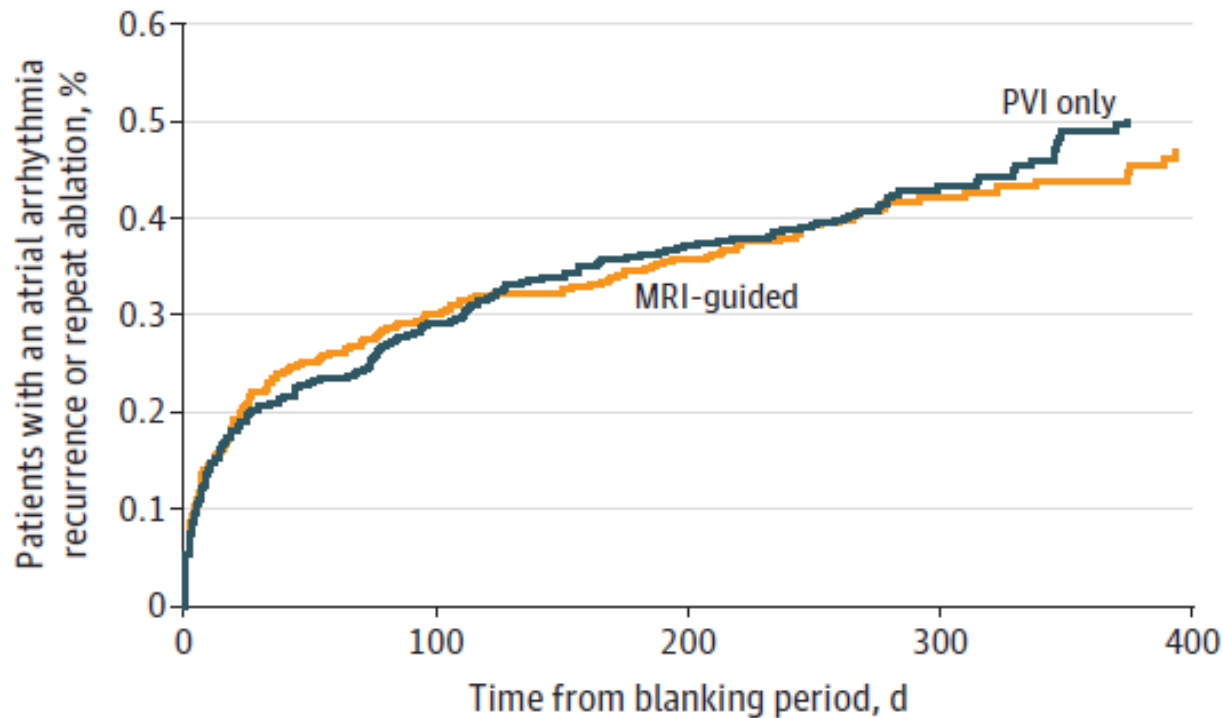


Table 1. Baseline Characteristics

Characteristic	No. (%)	
	MRI-guided (n = 421)	PVI only (n = 422)
Age, median (IQR), y	62.2 (57.0-68.2)	63.2 (57.1-68.8)
>75 y	24 (5.7)	24 (5.7)
Women	89 (21.1)	89 (21.1)
Men	332 (78.9)	333 (78.9)
Ethnicity, No. <sup>a</sup>	386	389
Hispanic or Latino	19 (4.9)	11 (2.8)
Not Hispanic or Latino	367 (95.1)	378 (97.2)
Race, No. <sup>a</sup>	396	398
Alaska Native, Native Hawaiian or Other Pacific Islander	0	3 (0.8)
Asian	2 (0.5)	0
Black or African American	4 (1.0)	4 (1.0)
White	390 (98.5)	391 (98.2)
History of tobacco use	147 (34.9)	164 (38.9)
Medical history		
Baseline fibrosis levels		
<10%	48 (11.4)	50 (11.8)
10%-<20%	198 (47)	196 (46.4)
20%-<30%	144 (34.2)	137 (32.5)
≥30%	31 (7.4)	39 (9.2)
Median (IQR)	18.4 (12.7-23.4)	18 (13.2-23.8)

# MRI-Guided Fibrosis Ablation; DECAAF II Trial

Figure 2. Primary Composite of Atrial Arrhythmia Recurrence or Repeat Ablation



No. at risk						
MRI-guided	407	277	251	114	64	
PVI only	408	284	249	118	69	

# MRI-Guided Fibrosis Ablation; DECAAF II Trial

Table 2. Efficacy Outcomes<sup>a</sup>

	No. (%)		Risk difference (95% CI) <sup>b</sup>	Hazard ratio (95% CI) <sup>c</sup>	P value <sup>d</sup>
	MRI-guided (N = 407)	PVI only (N = 408)			
Primary outcome					
Atrial arrhythmia recurrence or repeat ablation <sup>e</sup>	175 (43.0)	188 (46.1)	-0.016 (-0.078 to 0.048)	0.95 (0.77 to 1.17)	.63
Components of the primary outcome (atrial arrhythmia types) <sup>f</sup>					
Atrial fibrillation	129 (31.7)	147 (36.0)	-0.029 (-0.089 to 0.036)	0.90 (0.71 to 1.14)	.37
Atrial flutter	33 (8.1)	26 (6.4)	0.021 (-0.020 to 0.064)	1.30 (0.78 to 2.17)	.32
Atrial tachycardia	7 (1.7)	6 (1.5)	0.003 (-0.018 to 0.024)	1.18 (0.40 to 3.50)	.77
Secondary outcomes					
Atrial arrhythmia recurrence, repeat ablation, or new atrial arrhythmia medication <sup>e,g</sup>	183 (45.0)	196 (48.0)	-0.016 (-0.080 to 0.048)	0.95 (0.78 to 1.16)	.62
Repeat ablation <sup>h</sup>	57 (14.0)	72 (17.6)	-0.028 (-0.070 to 0.013)	0.80 (0.56 to 1.12)	.20
Post hoc outcome					
Atrial arrhythmia recurrence, repeat ablation, new atrial arrhythmia medication or cardioversion <sup>e,g</sup>	187 (45.9)	198 (48.5)	-0.013 (-0.076 to 0.052)	0.96 (0.79 to 1.17)	.69

# MRI-Guided Fibrosis Ablation; DECAAF II Trial

Table 3. Safety Outcomes in Total Population<sup>a</sup>

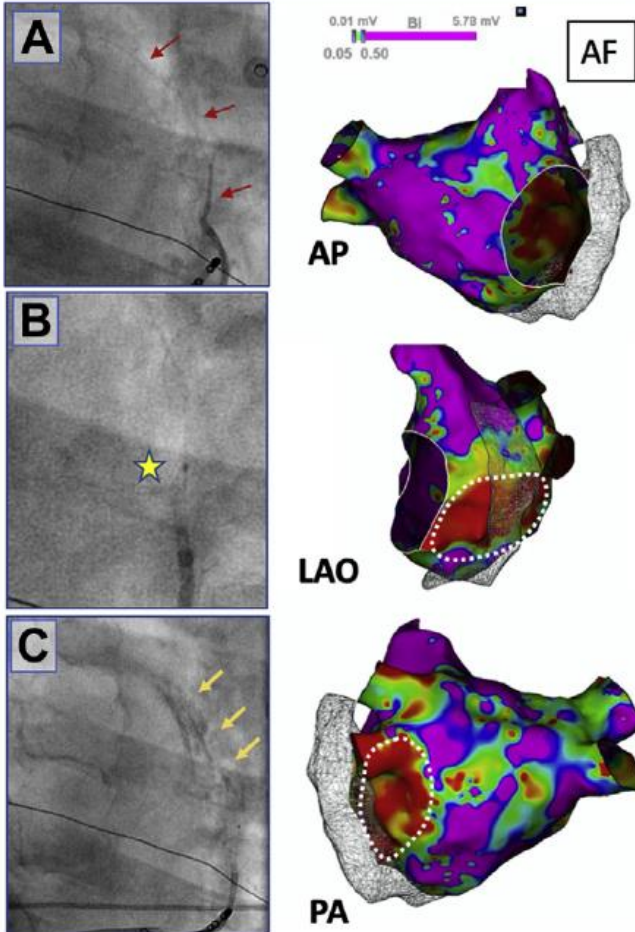
	No. (%)	
	MRI-guided (N = 403)	PVI alone (N = 428)
Safety outcomes		
Bleeding requiring transfusion	1 (0.2)	0
Heart failure	1 (0.2)	0
Pulmonary vein stenosis	0 (0)	0
Stroke or transient ischemic attack	6 (1.5)	0
Death	2 (0.5)	0
Primary composite safety outcome, defined as $\geq 1$ of the above events <sup>b</sup>	9 (2.2)	0
Esophageal injury <sup>c</sup>	5 (1.2)	1 (0.2)
Perforation or tamponade <sup>c</sup>	5 (1.2)	5 (1.2)

# Conclusion; MRI-Guided Fibrosis Ablation

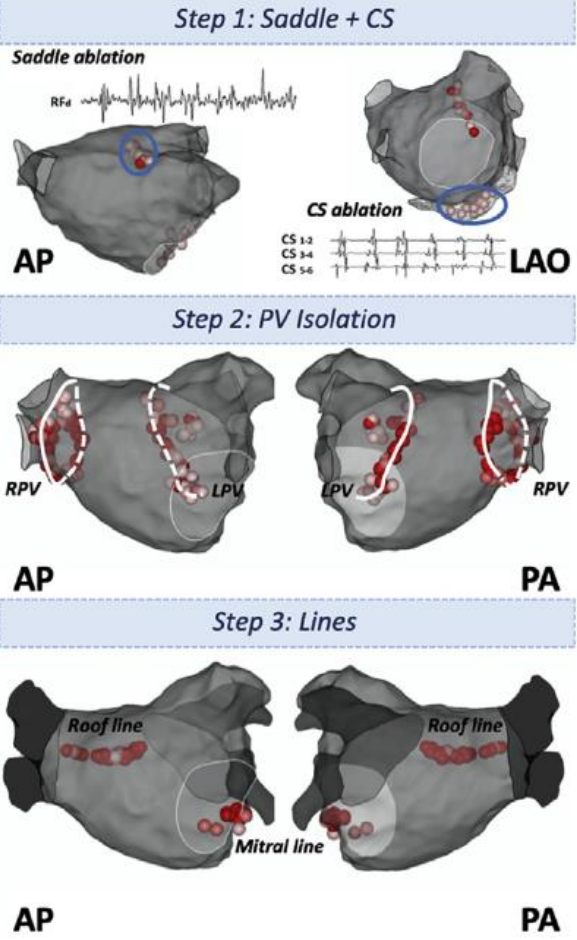
- In patients with persistent AF, MRI-guided fibrosis ablation plus pulmonary vein isolation resulted in no significant difference in recurrence of atrial arrhythmia compared with pulmonary vein isolation only.

# Marshall Bundle Elimination; Marshall Plan

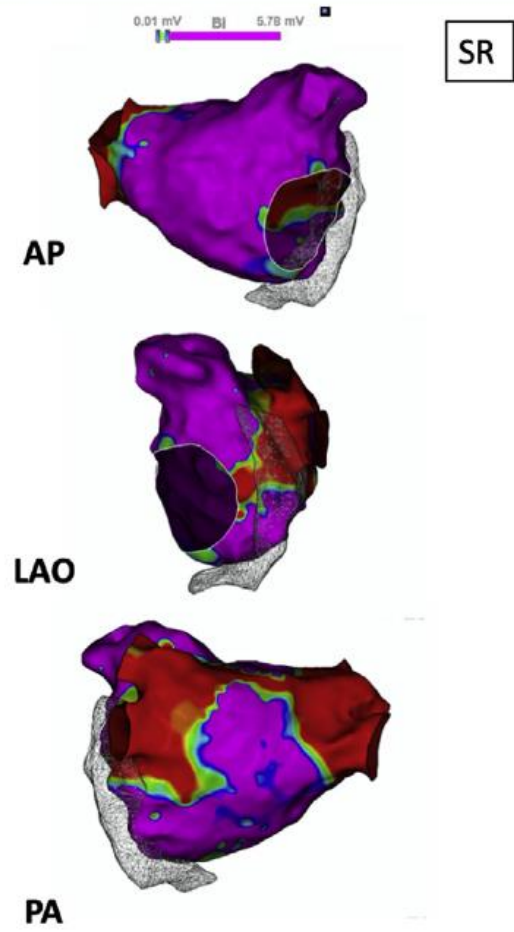
## VOM ethanol



## Ablation



## Final Voltage



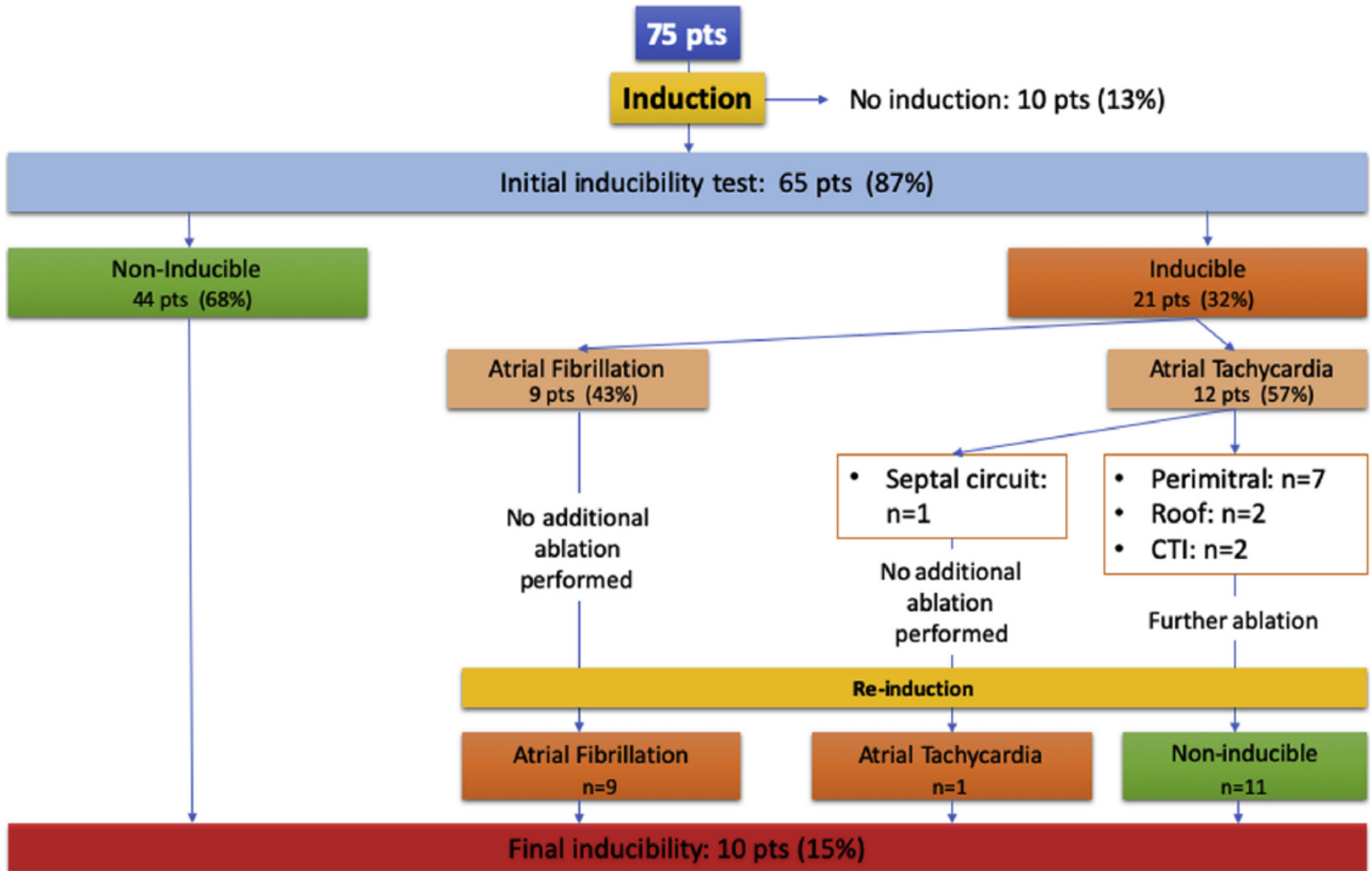


# Marshall Bundle Elimination; Marshall Plan

**Table 1** Baseline patient characteristics (N = 75)

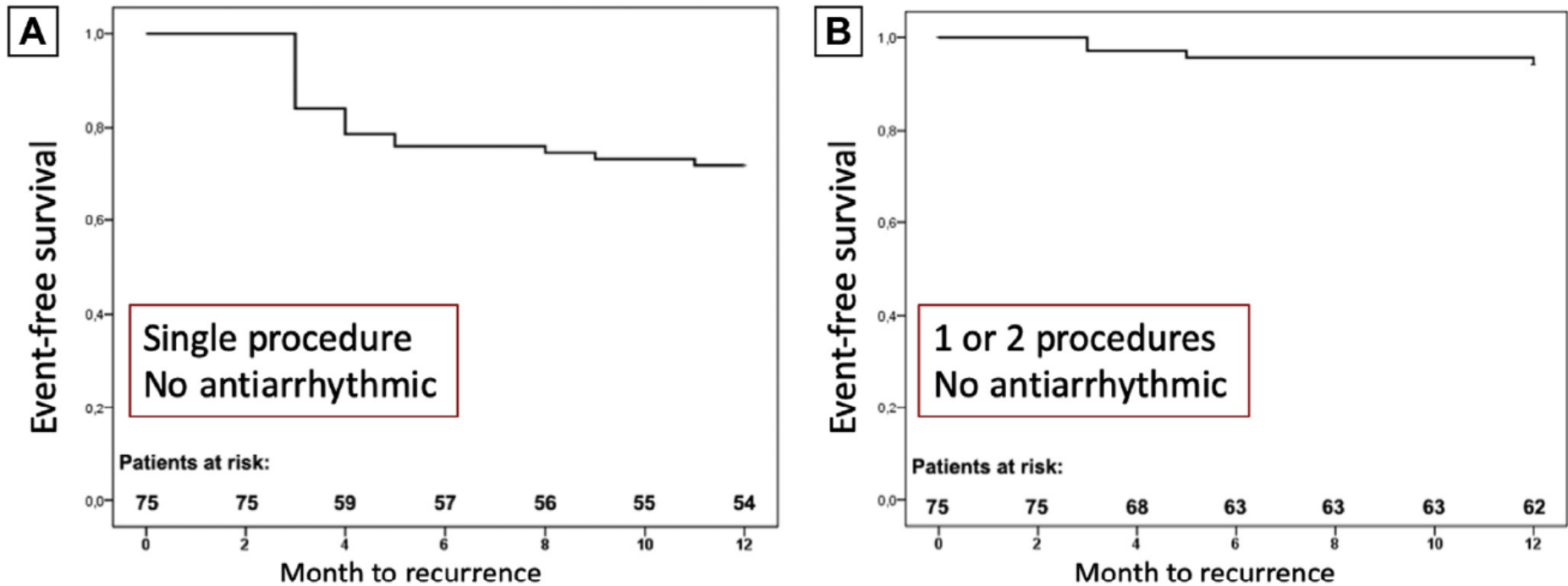
clinical characteristics	
Age (yr)	61 ± 9
Female	10 (13)
Structural heart disease	27 (36)
Hypertension	37 (49)
Heart failure	23 (32)
Previous stroke	4 (5)
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	1.7 ± 1.3
Amiodarone	48 (75)
Left ventricular ejection fraction (%)	54 ± 13
AF characteristics	
Maximum duration (mo)	9 ± 11
Longstanding AF	18 (24)
AF/AT at start of the procedure	45 (60)
Duration of current AF episode (mo)*	11 ± 11
History of cardioversion	64 (85)
Left atrial volume (cm <sup>3</sup> )	197 ± 43
Left atrial appendage cycle length (ms)	178 ± 35
Right atrial appendage cycle length (ms)	182 ± 35

# Marshall Bundle Elimination; Marshall Plan



# Marshall Bundle Elimination; Marshall Plan

## Freedom from AT/AF



**Figure 4** Freedom from atrial fibrillation (AF)/atrial tachycardia (AT). Kaplan-Meier event-free survival curves after a single ablation procedure, without antiarrhythmic drugs (A), and after 1 or 2 procedures, without antiarrhythmic drugs (B).

# Conclusion; Marshall Bundle Elimination

- In patients with persistent AF, the ablation strategy that systematically targets anatomical atrial structures (vein of Marshall ethanol infusion, pulmonary vein isolation, and linear lesions) is feasible, safe, and associated with a high rate of freedom from arrhythmia recurrence.

# Summary

- Low-voltage myocardium-guided ablation & Marshall bundle elimination may be effective and safe.
- Posterior wall isolation & MRI-guided fibrosis ablation may not be effective.
- MRI-guided fibrosis ablation may not be safe.

**Thank you**

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