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Summary

Catheter Ablation or Medical Therapy to Delay Progression of Atrial Fibrillation: The Randomized Controlled Atrial Fibrillation Progression Trial (ATTEST)

Kuck K-H, Lebedev DS, Mikhaylov EN, Romanov A, Gellér L, Kalējs O, Neumann T, Davtyan K, On YK, Popov S, Bongiorni MG, Schlüter M, Willems S, Ouyang F. *Europace*. Published online December 17, 2020. doi:10.1093/europace/euaa298.

STUDY QUESTION

Is RF catheter ablation more effective than AAD therapy alone in delaying the progression to persistent AF in patients with symptomatic paroxysmal AF?

METHODOLOGY

DESIGN:
PROSPECTIVE, MULTICENTER, RANDOMIZED, CONTROLLED, 2-ARM OPEN-LABEL STUDY

29
CENTERS

255
PATIENTS
≥60 years old with paroxysmal AF

INTERVENTIONS

Standard-of-Care AF Management

PVI with irrigated RF catheters
(n=128)

VS

AAD alone
(n=127)

OUTCOMES

PRIMARY OUTCOME

PROGRESSION TO PERSISTENT AF/AT

ADDITIONAL OUTCOMES

FACTORS ASSOCIATED WITH DISEASE PROGRESSION

RESULTS

Progression to persistent AF/AT was significantly lower in the RF ablation group at 3 years

2.4%
95% CI: 0.6–9.4%

VS

17.5%
95% CI: 10.7–27.8%

P=0009

Factors associated with persistent AF/AT disease progression

10x — **Less likely** to develop persistent AF/AT for patients treated with **RF ablation**
Hazard ratio: 0.107 (95% CI: 0.024–0.47; *P*=0.0031)

4x — **More likely** to develop persistent AF/AT for **patients ≥65 years old**
Hazard ratio: 3.87 (95% CI: 0.88–17.00; *P*=0.0727)

CONCLUSION

RF ablation is **superior** to guideline-directed AAD therapy alone in **delaying progression** from paroxysmal to **persistent AF.**

AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; CI, confidence interval; PVI, pulmonary vein isolation; RF, radiofrequency.

Kuck K-H, Lebedev DS, Mikhaylov EN, et al. Catheter ablation or medical therapy to delay progression of atrial fibrillation: The randomized controlled Atrial Fibrillation Progression Trial (ATTEST). *Europace.* Published online December 17, 2020. doi: 10.1093/europace/euaa298.

OBJECTIVE

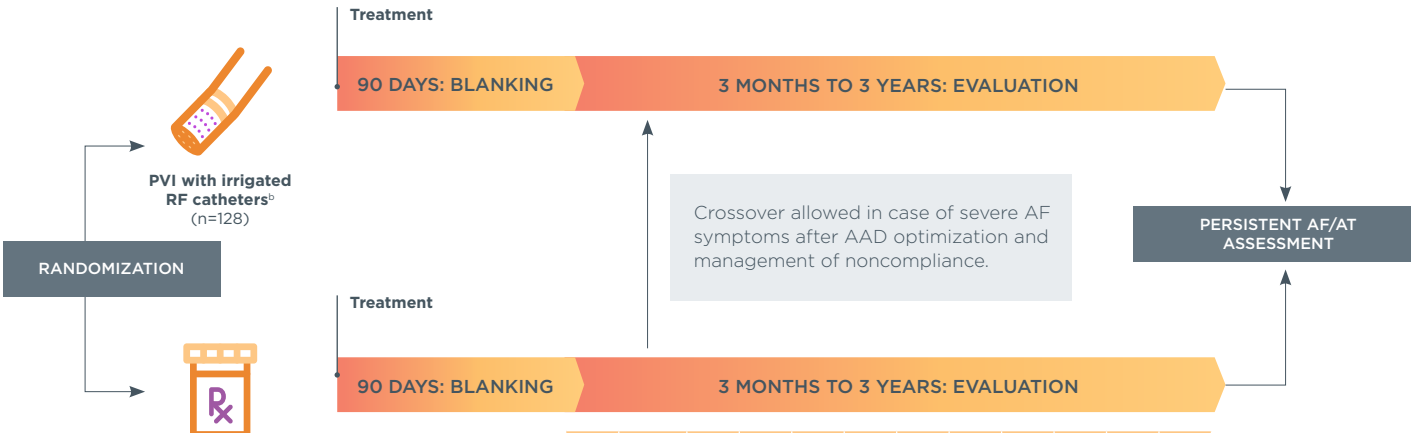
To evaluate if RF ablation is more effective than AAD therapy alone in delaying the progression to persistent AF over the course of 3 years in patients ≥60 years old with paroxysmal AF.

METHODS

Experimental Design

STUDY DESIGN	• Prospective, multicenter, randomized, controlled, 2-arm open-label study
STUDY PERIOD AND LOCATION	• February 2012 to May 2018 • 29 centers in 13 countries
INCLUSION CRITERIA	• 255 patients ≥60 years old with paroxysmal AF ≥2 years • ≥2 AF episodes over the 6 months preceding enrollment • Failed 1–2 AADs • HATCH score 1–4
PATIENT FOLLOW-UP	• Standard-of-care monitoring at 3 months, 6 months, 1 year, 2 years, and 3 years
PRIMARY ENDPOINT	• First documented occurrence of persistent AF/AT after a 90-day blanking period assessed at 3 years[a]
OTHER OUTCOMES	• Factors associated with disease progression • Time to recurrent AF/AT

Interventions Per Standard-of-Care Practice



	3M	6M	9M	1Y		1.5Y		2Y		2.5Y		3Y
OFFICE VISIT	x	x		x				x				x
ECG	x	x		x				x				x
PHONE FU			x			x				x		
TTM[c]	Weekly 3-8 months		Monthly 9 months to 3 years									

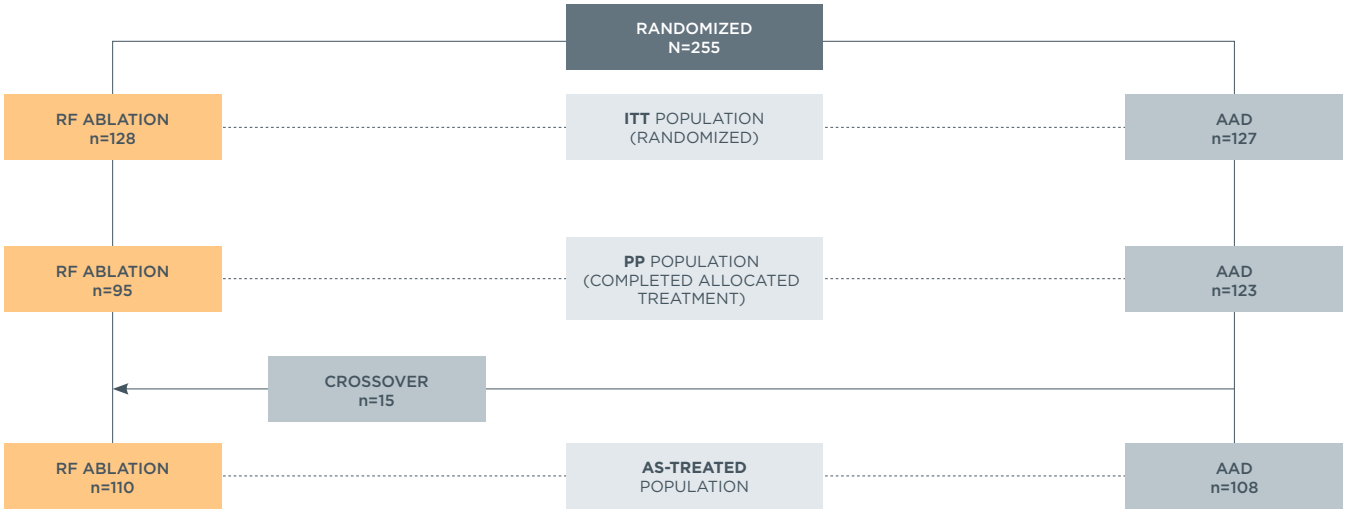
- Medications were managed for all patients in both groups per current treatment guidelines.
- Crossover from the AAD to the RF group was allowed for treatment-compliant patients who experienced severe side effects or AF symptoms when no other drug options were available.
  - To minimize crossover, noncompliant patients or those taking concurrent incompatible medications underwent medication management and reevaluation before the crossover was authorized.
- Due to budget constraints following slow enrollment, the trial was terminated prematurely by the sponsor in February 2018 after the second planned interim analysis; termination was independent of study outcomes.

AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; ECG, electrocardiogram; FU, follow-up; HATCH score, hypertension=1, age >75=1, transient ischemic attack or stroke=2, chronic obstructive pulmonary disease=1, Heart failure=2; PVI, pulmonary vein isolation; RF, radiofrequency; TTM, transtelephonic monitoring.

[a] Persistent AF was defined as episodes lasting for >7 consecutive days or requiring termination by cardioversion after 48 hours.
[b] RF ablation was performed with noncontact force-sensing and contact force-sensing catheters (NAVISTAR® THERMOCOOL® Catheter, THERMOCOOL® SF NAV Catheter Bi-Directional Navigation Catheter, THERMOCOOL SMARTTOUCH® Bi-Directional Navigation Catheter, THERMOCOOL SMARTTOUCH® Uni-Directional Navigation Catheter, NAVISTAR RMT THERMOCOOL® Catheter) in conjunction with a 3-dimensional electroanatomic mapping system (CARTO® 3, CARTO® XP, or CARTO® RMT),
[c] Transtelephonic monitoring transmission per specified schedule or whenever patients experienced symptoms. Once AF/AT was identified, daily TTM was initiated for 7 consecutive days.

RESULTS

Patient Disposition and Demographics



Demographics and baseline characteristics were generally similar between treatment groups.

PARAMETER	ITT POPULATION	
	RF ABLATION (n=128)	AAD (n=127)
Age, mean (SD), y	67.8 (4.8)	67.6 (4.6)
Male, No. (%)	54 (42.2)	53 (41.7)
Months since first experience of AF, median (range)	51.2 (19–625)	49.8 (25–366)
AF/AT episodes during prior 6 months, median (range)	6.5 (2–180)	6.0 (0–180)
Lone AF	38 (29.7)	39 (30.7)
HATCH score, mean (SD)	1.5 (0.9)	1.7 (0.9)
Left atrial diameter, mean (SD), mm	42.1 (6.1)	43.4 (5.6)
Left ventricular ejection fraction, mean (SD), %	61.8 (5.8)	62.3 (5.2)
AAD Class I/III at baseline	61 (47.7)	69 (54.3)
Medical history, No. (%)		
Hypertension	120 (93.8)	123 (96.9)
Hyperlipidemia/dyslipidemia	67 (52.3)	67 (52.8)
Left ventricular hypertrophy	26 (20.3)	23 (18.1)
Congestive heart failure	24 (18.8)	27 (21.3)
Atrial flutter	15 (11.7)	10 (7.9)
Diabetes	13 (10.2)	14 (11.0)
Transient ischemic attack/stroke	12 (9.4)	8 (6.3)
Cardiomyopathy[a]	6 (4.7)	2 (1.6)
Renal insufficiency	3 (2.3)	4 (3.1)

AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; HATCH score, hypertension=1, age >75=1, transient ischemic attack or stroke=2, chronic obstructive pulmonary disease=1, Heart failure=2; RF, radiofrequency; ITT, intention to treat; PP, per protocol.

[a]Includes ischemic, nonischemic dilated, and hypertrophic obstructive cardiomyopathy.

RESULTS

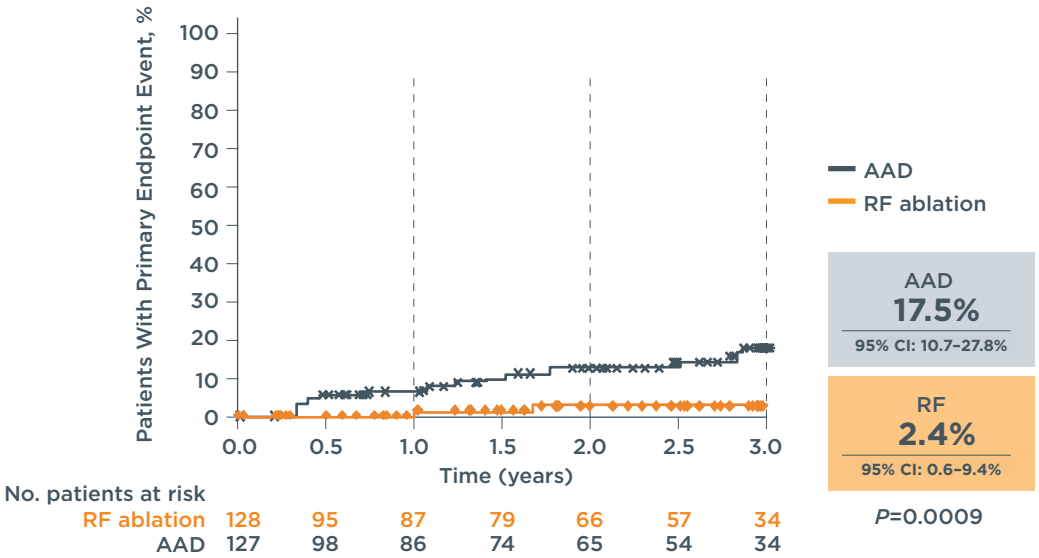
Intervention and Treatment

- Complete PVI was achieved in all patients who underwent RF ablation.
  - Noncontact force-sensing THERMOCOOL® Catheters were the most commonly used catheters (58.8%), followed by contact force-sensing THERMOCOOL SMARTTOUCH® Catheters (31.4%).
- Excluding beta-blockers and calcium channel blockers, 53 of 127 patients in the AAD group (41.7%) and 30 of 128 patients in the RF ablation group (23.4%) were initiated with new Class I/III AADs during the study.

Primary Efficacy

The superiority of RF treatment over AAD alone in delaying persistent AF/AT progression was observed at 1-year follow-up and strengthened by the 3-year follow-up.

Kaplan-Meier Estimate of Persistent AF/AT Progression (ITT Population)



- The primary efficacy analysis on the ITT population was confirmed for the PP population, As-Treated population, and when using the 2017 Heart Rhythm Society expert consensus definition of persistent AF.[1]

Kaplan-Meier Estimate of Persistent AF/AT Progression at 3 Years

	PP Population	As-Treated Population	ITT Population (2017 HRS)
RF ablation group	2.6%	2.2%	0.0%
vs			
AAD group	20.6%	20.6%	14.9%
P value	0.0003	<0.0001	0.0004

AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; HRS, Heart Rhythm Society; ITT, intention to treat; PP, per protocol; PVI, pulmonary vein isolation; RF, radiofrequency.

RESULTS

Factors Associated with AF Progression

Treatment modality and age were associated with AF progression in the PP population, suggesting that early RF ablation can delay disease progression.

Cox Model With Multiple Baseline Covariates and Treatment as the Time-Dependent Covariate

Patients treated with RF ablation

VS

Patients treated with AAD alone

RF ABLATION PATIENTS WERE APPROXIMATELY **10X LESS LIKELY** TO **PROGRESS** TO PERSISTENT AF/AT

Hazard ratio: 0.107 (95% CI: 0.024–0.47; *P*=0.0031)

Patients ≥65 years old

VS

Patients 60–64 years old

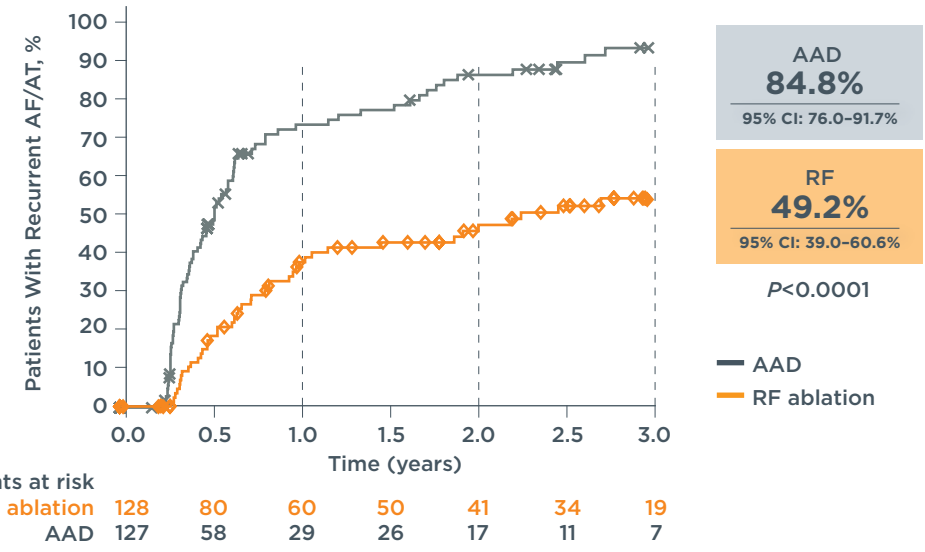
PATIENTS ≥65 YEARS OLD WERE ALMOST **4X MORE LIKELY** TO **PROGRESS** TO PERSISTENT AF/AT REGARDLESS OF TREATMENT ALLOCATION

Hazard ratio: 3.87 (95% CI: 0.88–17.00; P=0.0727)

Time to Recurrent AF/AT

The incidence of recurrent AF/AT was consistently lower with RF ablation than with AAD treatment from 6 months through the the end of the study.

Kaplan-Meier Estimate of Time to Recurrent AF/AT (ITT Population)



No. patients at risk

RF ablation	128	80	60	50	41	34	19
AAD	127	58	29	26	17	11	7

AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; ITT, intention to treat; PP, per protocol; RF, radiofrequency.

CONCLUSION

ATTEST demonstrated that **RF catheter ablation**—as part of standard-of-care AF management including AADs—is **superior to guideline-directed AAD therapy alone** in **delaying the progression to persistent AF** in patients with paroxysmal AF.

- Patients treated with **RF ablation** were **significantly less likely** to **develop persistent AF or persistent AT** than patients treated with AADs.
- **Patients ≥65 years** were **more likely to progress to persistent AF/AT** than patients <65.
- These results suggest that **early RF ablation** may be an **effective treatment strategy** for **delaying AF progression.**

REFERENCE

1. Calkins H, Hindricks G, Cappato R, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm* 2017;14:e275–e444.

AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; RF, radiofrequency.

Biosense Webster, Inc.
31 Technology Drive
Irvine, CA 92618 USA
Tel: +1-909-839-8500
Tel: +1-800-729-9010
www.biosensewebster.com

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