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ORIGINAL RESEARCH

Does Age Impact Safety and Efficacy During Pulse-Field Ablation for Atrial Fibrillation?

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BACKGROUND: There is no evidence evaluating efficiency, effectiveness, and safety outcomes in older patients in the context of pulsed-field ablation technology for the ablation of atrial fibrillation. We aimed to compare safety, efficacy, and acute and long-term outcomes of pulsed-field ablation in older patients (≥75 years) with younger ones.

METHODS: We enrolled consecutive patients who had undergone atrial fibrillation ablation with the pulsed-field ablation FARAPULSE system (Boston Scientific) at 15 centers. Patients were stratified by age (<65, 65–74, and ≥75 years) and efficacy and safety profiles of these groups were compared.

RESULTS: A total of 1082 patients were included: 108 (10%) were ≥75 years old, 374 (34.6%) were 65–74 years old and 600 (55.4%) were <65 years old. Older patients displayed a more pronounced risk profile compared with their younger counterparts, characterized by a significant higher burden of comorbidities. No differences in terms of procedural metrics were found. Pulmonary vein isolation was achieved in all patients. An overall low rate of procedural-related complications was reported (3.0%) without difference between young and older patients (P=0.241). During a mean follow-up of 342±111 days, a primary efficacy end point occurred in 605 of 748 (80.9%) patients with available outcome information. The arrhythmia recurrence rate ranged from 14.4% in patients <65 years old to 26.9% of older patients (P=0.011).

CONCLUSIONS: Drawing from these findings, using the FARAPULSE system for atrial fibrillation ablation in older patients demonstrated swift, safe, and effective acute outcomes, mirroring a comparable pattern observed in younger patients and recurrence rates in line with the literature in older patients.

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Key Words: age ■ atrial fibrillation ■ electroporation ■ older patients ■ pulsed-field ablation

The prevalence of atrial fibrillation (AF) increases progressively with age,[1,2] and the anticipated trend in the age distribution of AF within developed countries suggests a forthcoming shift, characterized by a projected rise in AF prevalence among the older population. Age represents a significant risk factor not only for the initial onset but also for the subsequent progression of AF from paroxysmal to persistent and

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CLINICAL PERSPECTIVE

What Is New?

- This is the first prospective observational multicenter study to assess efficacy and safety of the novel FARAPULSE pulsed-field ablation system in a large cohort of patients undergoing electroporation for atrial fibrillation with a focus on age, stratified into 3 groups: <65, 65–74 and ≥75 years old.
- Pulsed-field ablation for atrial fibrillation proved to be safe in patients with paroxysmal atrial fibrillation as well as those with persistent atrial fibrillation, regardless of age, with an overall low rate of complications.
- Age resulted as an independent predictor of arrhythmia recurrences: young patients (<65 years old) had a significantly lower arrhythmia recurrence rate and later recurrences than patients aged >65 years old, whereas no differences were found between young-older (65–74 years old) and older patients (≥75 years old).

What Are the Clinical Implications?

- This analysis indicates that older patients undergoing electroporation for atrial fibrillation achieve rapid, safe, and effective acute outcomes, with complication rates comparable to those observed in younger patients; these findings may guide treatment strategies to optimize health care resource utilization in this population.

Nonstandard Abbreviations and Acronyms

PFA	pulsed-field ablation
PVI	pulmonary vein isolation

permanent forms.[3,4] Thermal ablation, utilizing radiofrequency or cryoballoon, is an established strategy for AF.[4] Recent meta-analyses have shown comparable success rates in AF ablation, albeit with a notably elevated risk of complications observed in patients >75 years of age compared with their younger counterparts.[5–7]

A novel nonthermal ablation approach known as pulsed field ablation (PFA) has recently emerged, providing fast lesion creation through irreversible electroporation. There is limited evidence assessing the efficiency, effectiveness, and safety outcomes of PFA technology in older (>75 years) patients.[8–13] The aim of our analysis is to compare the safety and efficacy of PFA in older patients (≥75 years of age) to younger patients.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patient Population, Study Design, and End Points

The study used a prospective, nonrandomized, multicenter design. Between July 2022 and December 2023, a total of 1082 consecutive patients referred for paroxysmal and persistent AF ablation, who underwent the ablation procedure utilizing the novel FARAPULSE PFA system (Boston Scientific) across 15 Italian centers, were enrolled in the ATHENA (Advanced Technologies for Successful Ablation of AF in Clinical Practice) registry. In the present analysis, this population was stratified into 3 groups according to age named in this way: <65 years (young), between 65 and 74 years (young-older), and ≥75 years (older), and comparisons were made among groups. All patients were followed up at the enrolling center, from the time of first ablation to the last follow-up visit. The study protocol was carried out in accordance with the ethical principles established by the Declaration of Helsinki and was approved by the local ethics committee of our Institution. All patients provided written informed consent.

Ablation Procedure

All procedures were performed with patients under either deep conscious sedation or general anesthesia. The choice of anesthesia protocol was guided by the operator's preference, expertise, and the patient's overall health status.[11,12] Anticoagulation was administered in adherence to the most recent guidelines.[4] After the transseptal puncture, procedural activated clotting times were maintained at a minimum of 300 seconds through the administration of intravenous heparin bolus or continuous infusion. The procedure involved the utilization of the penta-splines 12F over-the-wire PFA catheter (FARAWAVE, Boston Scientific). Pulmonary vein isolation (PVI) was performed by means of 4 applications in a basket configuration and 4 applications in a flower configuration per pulmonary vein (PV), as described elsewhere.[8,11–13] Between pairs of PFA applications, the catheter was rotated by ≈30°/45° after the first 2 applications in each configuration, to cover the entire PV circumference. Additional lesion sets were deployed per physician's discretion. Ablation was performed by using an amplitude setting of 2.0 kV for each of the 4 PVs. The ablation end point was determined based on electrogram recordings, with the FARAWAVE catheter sequentially positioned in each PV. In cases of sinus rhythm, pacing from the coronary sinus was used to differentiate between the PV spike and the left atrial far-field electrograms.

Postablation Management

Regular follow-up assessments involved outpatient clinic visits at 1, 3, 6, and 12 months after the procedure, or whenever complaints arose. These assessments included a comprehensive history review, physical examination, 12-lead electrocardiogram, 24-hour or 7-day Holter monitoring, and screening for any adverse events. Postablation, both anticoagulation and antiarrhythmic drug therapies were continued. At the 3-month follow-up, the decision to continue anticoagulation was based on the stroke risk, while the continuation of antiarrhythmic drugs was at the treating physician's discretion. During the first 3 months following the ablation procedure (known as the blanking period), any occurrence of AF/atrial tachycardia was not considered a late recurrence. Additionally, episodes of atrial tachycardia or atrial flutter were also classified as recurrence. Significant adverse clinical events, encompassing cardiac tamponade, air embolism, stroke, transient ischemic attack, atrio-esophageal fistula, and mortality, were documented. The evaluation of the connection between each adverse event and the device and/or procedure was established by the respective participating center.

Statistical Analysis

Descriptive statistics are reported as means±SD for normally distributed continuous variables, or medians with 25th to 75th percentiles in the case of skewed distribution. Normality of distribution was tested by means of the nonparametric Kolmogorov–Smirnov test. Differences between mean data were compared by means of a *t* test for Gaussian variables, and the *F*-test was used to check the hypothesis of equality of variance. The Mann–Whitney nonparametric test was used to compare non-Gaussian variables. Differences in proportions were compared by applying χ^2 or Fisher exact test, as appropriate. Univariable Cox proportional hazards models were used to determine the association between patients' baseline characteristics and procedural parameters and the occurrence of atrial arrhythmia events during the follow-up period, and to estimate the hazard ratios with 95% CI. Variables with statistical significance (*P* value <0.05) were entered into a multivariable Cox regression model. The cumulative probability of arrhythmia recurrence was displayed by means of the Kaplan–Meier method, and the log-rank test was used to compare cumulative events. A *P* value <0.017 was considered significant after Bonferroni correction for multiple comparisons. All statistical analyses were performed by means of R: A language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population

Baseline clinical characteristics are reported in Table 1. The mean age was 62.7±10 (range 24–86 years), with 108 (10%) patients >75 years of age and 18 (1.7%) >80 years of age. In each group, most patients were male, with a notable increase in female representation observed with advancing age. Older patients displayed a more pronounced risk profile compared with their younger counterparts, characterized by a significant higher burden of comorbidities. Patients aged ≥75 years exhibited a significantly greater prevalence of coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease, history of cancer, and hypertension.

Procedural Characteristics and Acute Effectiveness

De novo PVI was performed in 945 patients (87.3%). Seven hundred forty-four procedures (68.8%) were performed with patients under general anesthesia, whereas deep sedation was applied in 338 (31.2%) patients. A 3D mapping system was used in 227 (21.0%) patients and intracardiac echocardiography in 288 (26.6%). At the end of the procedure, PVI was achieved in all (100%) patients (median number of PFA applications to achieve PVI=32 [32–40]). Additional lesions outside PVs were delivered in 268 (24.8%) cases (263 [24.3%] cases with PVI plus additional lesions and 5 [0.5%] cases with additional lesions only) with a median of 16 [95% CI, 12–20] PFA deliveries. Complete PVI was achieved in all patients, as was left atrial posterior wall isolation in patients who underwent left atrial posterior wall as additional lesion set, all validated through differential pacing and/or 3D mapping. Periprocedural details have been reported in Table 2. The overall median skin-to-skin time and catheter laboratory utilization (patient entering–leaving the Electrophysiology laboratory (EP) laboratory) were 63 [54–82] minutes and 75 [60–105] minutes, respectively; fluoroscopy time was 15 [12–21] minutes. No differences in terms of procedural metrics were found among groups (ie, skin-to-skin time, fluoroscopy time or time to PVI) except for a higher number of PFA deliveries outside of PVs in the young-older group (*P*=0.009 versus young and *P*=0.017 versus older) (Table 2 and Figure S1A and S1B). Catheter laboratory utilization was <120 minutes and 90 minutes in 82.5% (ranging from 84.8% in young patients to 78.7% in older patients, *P*=0.118) and 69% (ranging from 71.3% in young patients to 66.0% in young-older patients, *P*=0.087) of the cases, respectively (Figure 1A). Skin-to-skin time was <90 minutes and 60 minutes in 83.4% (ranging from 85.3% in young patients to 80.6% in older patients, *P*=0.246) and

Table 1. Baseline Clinical Characteristics of the Study Population

Parameter	Overall population (n=1082)	(A) Age <65 y (n=600)	(B) 65 y ≤ Age <75 y (n=374)	(C) Age ≥75 y (n=108)	*P* (A vs B)	*P* (A vs C)	*P* (B vs C)
Age, y	62.7±10	55.9±7	69.3±3	77.5±3	<0.0001*	<0.0001*	<0.0001*
Female sex, n (%)	299 (27.6)	123 (20.5)	137 (36.6)	39 (36.1)	<0.0001*	<0.0001*	1.00
Indication for ablation							
Paroxysmal AF, n (%)	723 (66.8)	419 (69.8)	234 (62.6)	70 (64.8)	0.0208	0.3099	0.7345
Early persistent AF, n (%)	273 (25.2)	136 (22.7)	112 (29.9)	25 (23.1)			
Long-standing persistent AF, n (%)	86 (7.9)	45 (7.5)	28 (7.5)	13 (12.0)			
History of AT/AFL, n (%)	81 (7.5)	49 (8.2)	24 (6.4)	8 (7.4)	0.3812	1.00	0.6662
LVEF, %	57.3±8	57.4±7	56.6±8	59.4±7	0.4754	0.0241	0.0643
LAVi, mL/m^2	38.7±13	37.3±13	40.0±14	40.6±12	0.0715	0.0321	0.6403
Structural heart disease, n (%)	76 (7.0)	30 (5.0)	41 (11.0)	5 (4.6)	0.6662	1.00	0.0613
Coronary artery disease, n (%)	91 (8.4)	28 (4.7)	44 (11.8)	19 (17.6)	<0.0001*	<0.0001*	0.1434
History of heart failure, n (%)	42 (3.9)	25 (4.2)	14 (3.7)	3 (2.8)	0.8669	0.7873	0.7728
CKD, n (%)	20 (1.8)	7 (1.2)	6 (1.6)	7 (6.5)	0.5764	0.0022*	0.0122*
COPD, n (%)	33 (3.0)	9 (1.5)	17 (4.5)	7 (6.5)	0.0067*	0.0056*	0.4511
Stroke/TIA, n (%)	23 (2.1)	9 (1.5)	11 (2.9)	3 (2.8)	0.1622	0.4071	1.00
Hyperthyroidism, n (%)	41 (3.8)	20 (3.3)	17 (4.5)	4 (3.7)	0.3894	0.7750	1.00
History of cancer, n (%)	46 (4.3)	17 (2.8)	20 (5.3)	9 (8.3)	0.0572	0.0104*	0.2543
Sleep apnea, n (%)	46 (4.3)	30 (5.0)	12 (3.2)	4 (3.7)	0.1979	0.8063	0.7642
Diabetes, n (%)	149 (13.8)	70 (11.7)	58 (15.5)	21 (19.4)	0.0972	0.0408	0.3757
Hypertension, n (%)	508 (47.0)	234 (39.0)	209 (55.9)	65 (60.2)	<0.0001*	<0.0001*	0.4422
Hyperlipidemia, n (%)	311 (28.7)	154 (25.7)	140 (37.4)	37 (34.3)	0.0001*	0.0769	0.5728
History of major bleeding, n (%)	8 (0.7)	2 (0.3)	3 (0.8)	3 (2.8)	0.3779	0.0274	0.1293
Antiarrhythmics, n (%)	494 (45.7)	264 (44.0)	180 (48.1)	50 (46.3)	0.2098	0.6749	0.7443
β-blockers, n (%)	502 (46.4)	263 (43.8)	189 (50.5)	50 (46.3)	0.0475	0.6742	0.4467

AF indicates atrial fibrillation; AFL, atrial flutter; AT, atrial tachycardia; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; LAVi, left atrial volume indexed; LVEF, left ventricular ejection fraction; and TIA, transient ischemic attack.

*P <0.017 was considered significant after Bonferroni correction.

49.5% (ranging from 52% in young patients to 42.6% in older patients, P=0.076) of the cases, respectively (Figure 1B).

Long-Term Ablation Outcome and Predictors of AF/Atrial Tachycardia Recurrence During Follow-Up

Over a median follow-up of 364 [95% CI, 239–407] days, primary efficacy end point occurred in 605 of 748 (80.9%) patients with available outcome information (median time to recurrence: 186 [95% CI, 133–244] days). At multivariate logistic analysis adjusted for baseline confounders (Table 3), age (hazard ratio=1.03 [95% CI, 1.01–1.05]; P=0.0043) remained associated with atrial arrhythmias recurrence during follow-up. The arrhythmia recurrence rate ranged from 14.4% in young patients to 26.9% of older patients (P=0.011 versus young patients). Older and young-older patients exhibited a similar arrhythmia recurrence rate (24.6% for young-older, P=0.658 versus older patients). Figure 2 shows the Kaplan–Meier estimates of time to AF recurrence during follow-up, according to young, young-older, and older patients. The time to recurrence was longer in younger patients than in young-older and older patients (overall log-rank P=0.0005).

Periprocedural Complications

Overall complications occurred in 33 (3.0%) patients, ranging from 2.7% in the young-older patients, 2.8% in the young patients, to 5.6% in the older patients, showing no significant differences between the groups (odds ratio=2.02 [95% CI, 0.78–5.24], P=0.14 for older versus younger patients, odds ratio=2.14 [95% CI, 0.76–6.03]; P=0.15 for older versus young-older

Table 2. Procedural Characteristics

Parameter	Overall population (n=1082)	(A) Age <65 y (n=600)	(B) 65 y ≤ Age <75 y (n=374)	(C) Age ≥75 y (n=108)	*P* (A vs B)	*P* (A vs C)	*P* (B vs C)
Ablation approach							
De novo, n (%)	945 (87.3)	517 (86.2)	327 (87.4)	101 (93.5)	0.6284	0.0401	0.0846
Repeated ablation, n (%)	137 (12.7)	83 (13.8)	47 (12.6)	7 (6.5)			
Anesthesia protocol							
GA, n (%)	744 (68.8)	406 (67.7)	257 (68.7)	81 (75.0)	0.7775	0.1432	0.2336
Deep sedation, n (%)	338 (31.2)	194 (32.3)	117 (31.3)	27 (25.0)			
Ablation target							
PVI only, n (%)	814 (75.2)	470 (78.3)	272 (72.7)	72 (66.7)	0.0531	0.0131*	0.2284
PVI plus additional lesions, n (%)	263 (24.3)	129 (21.5)	98 (26.2)	36 (33.3)			
Additional lesions only, n (%)	5 (0.5)	1 (0.2)	4 (1.1)	0 (0.0)			
Mapping system used, n (%)	227 (21.0)	131 (21.8)	74 (19.8)	22 (20.4)	0.4678	0.8003	0.8917
Intracardiac echocardiography, n (%)	288 (26.6)	137 (22.8)	111 (29.7)	40 (37.0)	0.1017	0.0094*	0.1459
LA anatomy variants, n (%)	72 (6.7)	41 (6.8)	24 (6.4)	7 (6.5)	0.0747	1.00	0.579
Catheter laboratory utilization (patient entering–leaving the EP laboratory), min	75 [60–105]	70 [60–100]	77 [63–115]	80 [65–120]	0.0076*	0.0321	0.6403
Skin-to-skin (primary operator) time, min	63 [54–82]	60 [50–80]	65 [55–85]	65 [55–85]	0.0866	0.1449	0.6601
Total fluoroscopy time, min	15 [12–21]	15 [12–21]	16 [12–21]	16 [12–23]	0.4082	0.1931	0.4347
Time to PVI, min	19 [14–25]	20 [15–25]	18 [14–25]	20 [14–25]	0.6334	0.7207	0.5443
Number of PFA deliveries, n	36 [32–48]	34 [32–47.5]	36 [32–48]	38 [32–48]	0.0383	0.0808	0.6742
Number of PFA deliveries at PVs, n	32 [32–40]	32 [32–40]	32 [32–40]	32 [32–40]	0.5408	0.6082	0.8736
Number of PFA deliveries outside of PVs, n	16 [12–20]	15.5 [12–20]	18 [13–22]	14 [12–18]	0.0094*	0.5395	0.017*

EP, Electrophysiology; GA, general anesthesia; LA, left atrium; PFA, pulsed-field ablation; PVs, pulmonary veins; and PVI, pulmonary vein isolation.
*P <0.017 was considered significant after Bonferroni correction.

patients, respectively). No patient >80 years of age experienced a complication. The rate of major complications was 0.3% and consisted of 2 pericardial tamponades (0.2%, both not definitely associated with the use of PFA) and 1 transient ischemic attack (0.1%). No esophageal complications, PV stenosis, persistent phrenic nerve injury, or anesthesia-related complications were reported. Minor complications were reported in 30 patients (2.8%) after the procedure, predominantly related to vascular accesses or catheterization (n=14, 1.3%). Two coronary spasms were induced during PFA deliveries into the left inferior pulmonary vein and left superior pulmonary vein. No ventricular arrhythmias developed and both events resolved within a few seconds following the administration of nitrates. Details are reported in Table 4.

DISCUSSION

Main Findings

This prospective observational multicenter study is the first to assess efficacy and safety of the novel FARAPULSE PFA system in a large cohort of patients undergoing electroporation for AF with a focus on age. This analysis yielded several noteworthy findings: (1) PFA for AF proved to be safe in patients with paroxysmal AF as well as patients with persistent AF, regardless of age. Our data highlighted a low rate of complications (3.0%), mostly minor (2.8%), with no difference between young and older patients. (2) Young patients (<65 years) had a significantly lower arrhythmia recurrence rate and later recurrences than older patients (≥65 years), whereas no differences were found between young-older (65–74 years) and older patients (≥75 years). (3) 80.9% of patients remained free from arrhythmia recurrences during follow-up, with age remaining an independent predictor of arrhythmia recurrences even after adjusting for confounders (hazard ratio=1.03 [95% CI, 1.01–1.05]; P=0.0043)

Safety Profile

Catheter ablation for AF represents a sophisticated electrophysiological intervention. Given its invasive character necessitating vascular access, precise catheter manipulation, and energy deployment within the thin-walled left atrium proximate to adjacent organs

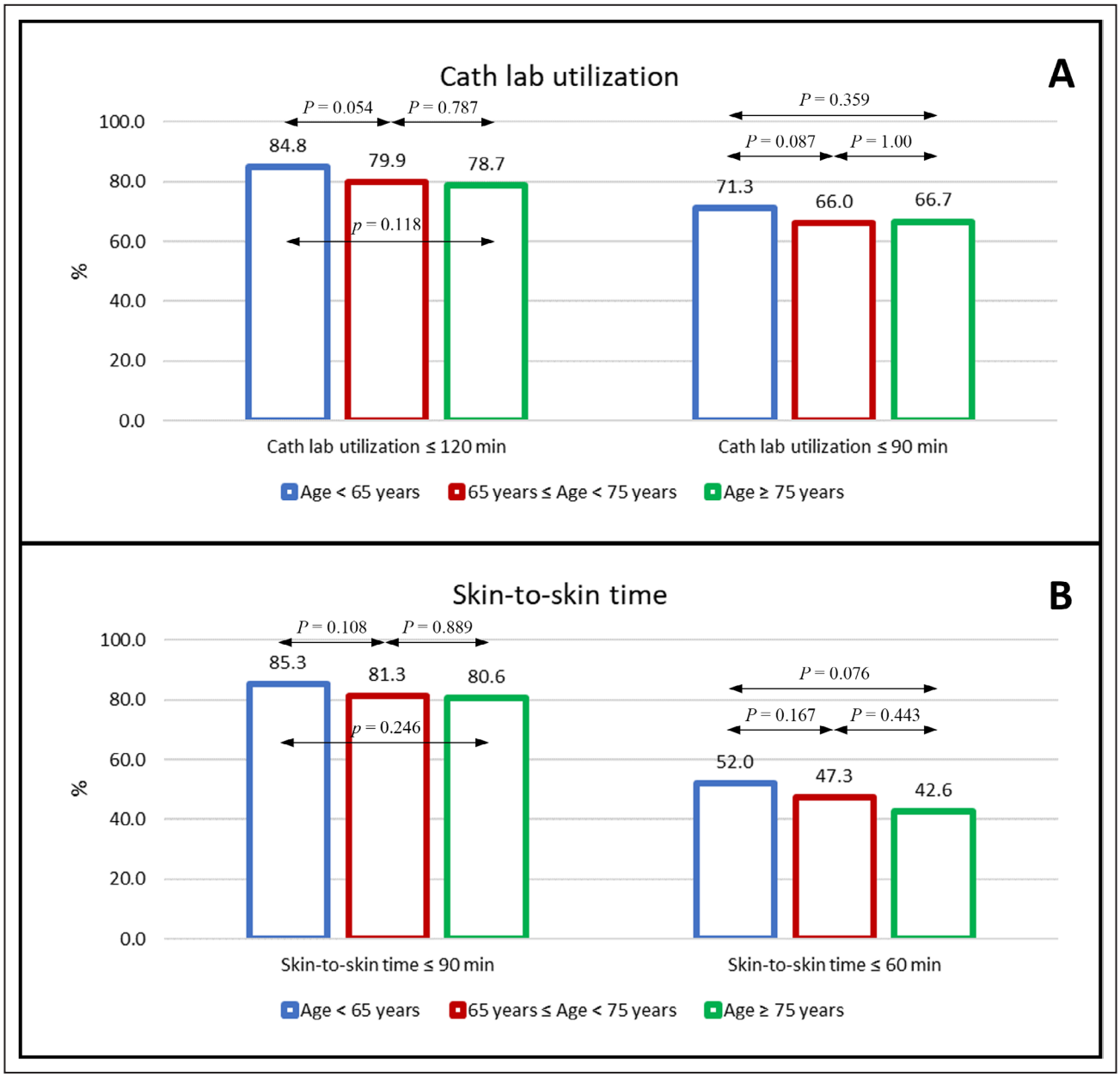

Figure 1. Percentage of patients, stratified by age, for catheter laboratory utilization and skin-to-skin time.
Percentage of patients for whom catheter laboratory utilization was ≤ 120 minutes or ≤ 90 minutes (**A**) and the percentage of patients for whom skin-to-skin time was ≤ 90 minutes or ≤ 60 minutes (**B**).

vulnerable to thermal injury, AF ablation carries a notable risk of complications, posing more significant concerns in a fragile cohort composed of older patients. This aspect assumes paramount significance considering that the primary objective of the procedure is usually symptom improvement[5] (especially during exercise, and quality of life amelioration) and these aspects being more difficult to establish and achieve in the older population, with several comorbidities jeopardizing physicians' assessment. Complication rates in patients undergoing catheter ablation for AF using thermal energy range from 4% to 14%, with 2% to 3% at risk of life-threatening outcomes.[14,15] In a recent large comprehensive study investigating PFA for AF,[16] major complications were detected in 1.6% of patients, while minor complications, mainly vascular in nature, were observed in 3.9% of cases.[17]

Our multicenter experience with PFA for AF revealed a markedly favorable safety profile, evidenced by a low overall complication rate (3.0%). Notably, only 0.3% of patients encountered major adverse events, including 2 cases of pericardial tamponade and 1 transient ischemic attack. Importantly, no complications could definitively be attributed to the electroporation

Table 3. Univariate and Multivariate Predictors of Any Atrial Arrhythmia Recurrence at 1-Year Follow-Up

	Univariate analysis			Multivariate analysis		
Variable	HR	95% CI	*P*	HR	95% CI	*P* value
Ablation target: PVI only	1.29	0.91–1.86	0.1538			
AF type (paroxysmal vs persistent)	0.95	0.67–1.35	0.7764			
Age	1.03	1.01–1.05	0.0029	1.03	1.01–1.05	0.0043
Antiarrhythmics	1.19	0.86–1.66	0.2885			
β-blockers	0.85	0.61–1.18	0.3404			
CAD	1.27	0.75–2.17	0.3771			
CKD	1.92	0.71–5.15	0.2002			
COPD	1.69	0.83–3.44	0.1487			
Deep sedation vs general anesthesia	0.72	0.50–1.05	0.0924			
Diabetes	1.11	0.71–1.74	0.637			
Female sex*	1.59	1.13–2.23	0.0076			
History of AT/AFL	1.47	0.84–2.60	0.1818			
History of cancer	1.49	0.79–2.82	0.2246			
History of HF	0.75	0.24–2.33	0.6175			
Hyperlipidemia	1.06	0.75–1.50	0.7585			
Hypertension	1.19	0.86–1.65	0.3025			
Hyperthyroidism	1.17	0.55–2.49	0.6901			
Intracardiac echocardiography*	1.46	1.04–2.03	0.0277			
LA anatomy variants	1.69	0.98–2.93	0.0622			
Left atrial volume	1.01	0.99–1.02	0.0615			
LVEF	1.01	0.98–1.04	0.5219			
Mapping system used	1.02	0.68–1.54	0.9159			
Number of PFA deliveries	1.01	0.99–1.03	0.1432			
Number of PFA deliveries at PVs	1.01	0.99–1.04	0.2386			
Repeated ablation	1.43	0.90–2.27	0.1284			
Sleep apnea	2.47	1.40–4.36	0.002	1.61	0.75–3.47	0.2232
Structural heart disease	0.67	0.32–1.43	0.3066			

AF indicates atrial fibrillation; AFL, atrial flutter; AT, atrial tachycardia; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; HF, heart failure; HR, hazard ratio; LA, left atrium; LVEF, left ventricular ejection fraction; PFA, pulsed-field ablation; PVs, pulmonary veins; and PVI, pulmonary vein isolation.

*Female sex at the time of the procedure and the use of intracardiac echocardiography were not entered into multivariate model due to correlation with age (female sex: Spearman's coefficient of rank correlation ρ=0.172; 95% CI, 0.11–0.23, *P* <0.0001; Kendall's τ=0.166; 95% CI, 0.11–0.22, *P* <0.0001; intracardiac echocardiography: ρ=0.104; 95% CI, 0.05–0.16, *P* <0.0001; τ=0.1; 95% CI, 0.05–0.16, *P* <0.0001).

energy source. Moreover, minor complications (2.8%) following the procedure primarily stemmed from vascular access or catheterization, aligning with existing literature.[5]

In addition to that, the rates of vascular complications are increased in the presence of concomitant disorders often associated with older age, and they are not attributable to the use of a specific ablation technology such as PFA.[18]

In the context of AF ablation, older patients had a higher susceptibility to postprocedural complications compared with younger patients, as anticipated.[6] Consistent with extensive observational studies conducted on population cohorts, advancing age correlates proportionally with adverse end points. As individuals age, physiological and anatomical changes increase their susceptibility to complications arising from catheter ablation procedures. Remarkably, we did not observe variations in safety profiles among distinct age groups, with overall complication rates ranging from 2.7% to 5.6% albeit with a trend towards older patients. It is important to note that the majority of complications are vascular in nature (0.9%), and these tend to be more common in older patients (in our study they ranged from 0.5% in patients <65 years to 3.7% in patients ≥75 years), regardless of the energy source used, but are associated with the use of large-sized sheaths. Notably, cardiac-related complications were comparable across all 3 groups. One of the most likely explanations is that the utilization of additional trigger ablation

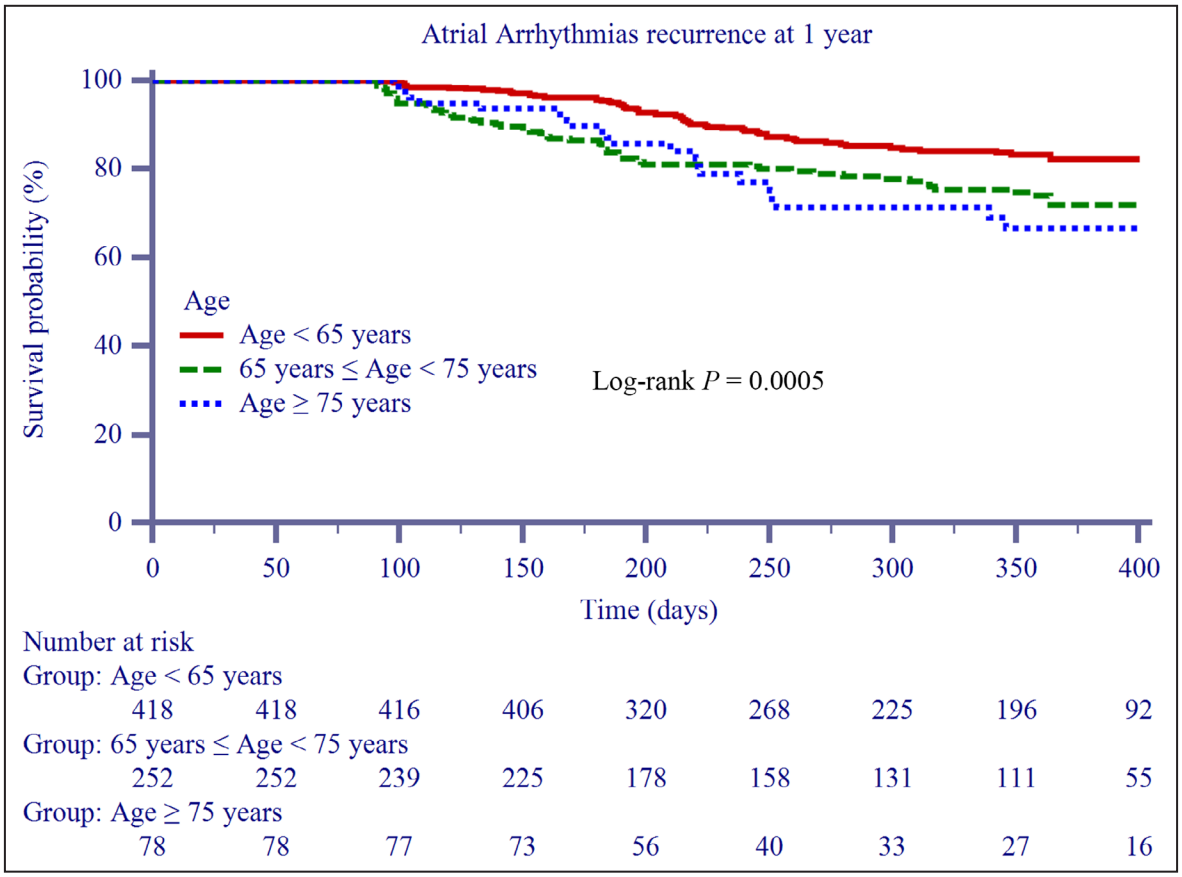

Figure 2. Survival curve from AF/AT recurrence during follow-up after the 90-day blanking period, according to young, young-older, and older patients.
AF indicates atrial fibrillation; and AT, atrial tachycardia.

techniques beyond PVI, more frequently used in older patients, potentially contributes to increased adverse outcomes of thermal ablation.[6] In line with this observation, our older cohort underwent an ablation strategy entailing a broader lesion set compared with younger patients; nevertheless, no disparities were noted based on age demographics, and this might be explainable by the well-known myocardial selectivity of PFA.

Efficiency and Efficacy Profile

The assessment of catheter ablation outcomes in older patients with AF remains inconclusive due to the limited sample sizes in existing studies, variations in ablation methodologies, and heterogeneous patient selection criteria.[6,7] The potential benefits of catheter ablation for older patients, particularly those >75 years old, compared with younger counterparts remain uncertain, primarily due to the exclusion or underrepresentation of this older demographic in clinical trials.[19] Consequently, the available published data show conflicting results regarding the efficacy of catheter ablation in the aged.

Heeger et al,[20] comparing patients aged 65–74 versus ≥75 years after AF cryoballoon ablation, showed no statistical difference between age groups (38.8% versus 38.7%). This percentage of recurrences was to be expected, because several studies have shown similar re-occurrence of AF after 1 ablation procedure.[20–22] Based on our findings, even in our population there were no statistically significant differences in terms of arrhythmia recurrences during follow-up between patients aged 65 to 74 years and patients aged ≥75 years. However, younger patients had a significantly lower arrhythmia recurrence rate and later recurrences than older patients, using a 65-years cut-off. This finding has been confirmed even after normalizing for confounders (eg, comorbidities).

Notably, the Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation trial[23] revealed an age-related disparity in clinical outcomes between ablation and antiarrhythmic drug therapy, with the greatest relative and absolute prognostic benefit observed in patients <65 years of age, suggesting potential clinical benefits of catheter ablation for select patient subgroups.

Table 4. Procedural Complications

Complications	Overall population (n=1082)	(A) Age <65 y (n=600)	(B) 65 y ≤ Age <75 y (n=374)	(C) Age ≥75 y (n=108)
Major complications, n (%)	3 (0.3)	1 (0.2)	1 (0.3)	1 (0.9)
Cardiac/Pericardial tamponade, n (%)	2 (0.2)	1 (0.2)	0 (0.0)	1 (0.9)
Stroke, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TIA, n (%)	1 (0.1)	0 (0.0)	1 (0.3)	0 (0.0)
Phrenic nerve injury (persistent), n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Acute kidney injury, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Minor complications, n (%):	30 (2.8)	16 (2.8)	9 (2.4)	5 (4.6)
Pericarditis, n (%)	7 (0.6)	3 (0.5)	3 (0.8)	1 (0.9)
Pseudoaneurysm, n (%)	6 (0.6)	4 (0.7)	2 (0.5)	0 (0.0)
Hematoma/Skin related, n (%)	4 (0.4)	2 (0.3)	1 (0.3)	1 (0.9)
Vascular-minor AEs, n (%)	4 (0.4)	1 (0.2)	1 (0.3)	2 (1.8)
Pericardial effusion without intervention, n (%)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)
Coronary spasm, n (%)	2 (0.2)	1 (0.2)	1 (0.3)	0 (0.0)
Arteriovenous fistula, n (%)	2 (0.2)	1 (0.2)	0 (0.0)	1 (0.9)
Pneumonia, n (%)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)
Other, n (%)	3 (0.3)	2 (0.3)	1 (0.3)	0 (0.0)
All complications, n (%)	33 (3.0)	17 (2.8)	10 (2.7)	6 (5.6)

AEs, Adverse events; and TIA, transient ischemic attack.

In addition to that, age is a significant factor in the development of extensive atrial fibrosis, which is linked to a reduced likelihood of successful AF ablation,[24] and our study also confirmed previous observations that older patients presented more frequently with extra-PV triggers or low voltage areas necessitating additional left atrial ablations.[20–22]

Moreover, older patients exhibited a higher burden of comorbidities such as chronic kidney disease, chronic obstructive pulmonary disease, and coronary artery disease, underscoring the need for extended catheter laboratory utilization due to the inherent complexity of their cases. However, it is noteworthy that procedural, fluoroscopy, and ablation times were comparable between older and younger patient cohorts.

Given these considerations, age alone should not serve as a decisive factor in determining candidacy for AF ablation, particularly when considering potential benefits such as reduced incidence of cardioembolic events and dementia[25] associated with AF ablation, in patients who may exhibit contraindications for oral anticoagulation more frequently.

Clinical Perspective

Currently, there is uncertainty regarding whether a particular technology for AF catheter ablation should be prioritized in older patients owing to its potentially improved safety profile.[5]

Ikenouchi et al,[26] in a propensity-matched comparison of older patients ≥75 years, reported that cryoballoon ablation was associated with similar efficacy and safety, but with shorter procedural time when compared with radiofrequency ablation. In a recent meta-analysis[6] considering the different strategies used for AF ablation and complications, Prasitlumkum et al[6] did not find any differences in complication rates in patients >75 years or <75 years who underwent cryoballoon ablation. On the other hand, greater risks were noticed in the older group (>75 years) in patients undergoing radiofrequency ablation. Yet, the question of whether cryoablation is safer for older patients remains unsettled, given that most of the studies included in this meta-analysis did not furnish data specifically intended for subanalyses in this demographic. Although our study is the first one assessing this topic, the question remains unsolved also in the context of PFA. While there are abundant data from single-center studies or randomized multicenter trials on the increased safety and efficacy adopting PFA rather than pure thermal energy only,[8,13,27–30] there is currently no specific assessment considering various age groups.

Although we did not conduct a comparative assessment among different technologies, our findings have important clinical implications, because they

demonstrate that older patients can still benefit from AF ablation with this novel therapy. Some medical centers might refrain from offering ablation therapy to older patients due to a perceived less favorable risk-to-benefit ratio associated with catheter ablation in this demographic.[19] In our study, in terms of procedural efficiency, most older patients underwent procedures lasting <90 minutes, although including cases from the introduction of PFA to until now, meaning that overall ablation times might also have been hampered by first cases performed by inexperienced operators in the PFA system. This aspect is significant when considering frail patients, often burdened with multiple comorbidities, requiring specific attention and precautions for optimal procedure management. In our cohort, older patients, in addition to being burdened by a higher prevalence of comorbidities, exhibited greater renal and respiratory compromise, crucial factors in procedural management. Despite these challenges, no additional complications arose, and outcomes were satisfactory, aligning with existing literature for this patient demographic.

Additional evaluations comparing different technologies in a specific older population are imperative to definitively clarify which strategy may be the best, both in terms of effectiveness and safety, for a subset of patients with more comorbidities and potential risk of increased complications.

Limitations

The principal limitations of this study arise from its intrinsic nonrandomized design. Nevertheless, the study was conducted prospectively, adhering to the standard-of-care protocols at each participating center for AF ablation and patient management. Moreover, the ATHENA study was designed to evaluate the real-world application and integration of a specific ablation technology within a heterogeneous population of patients with AF. Additionally, the proportion of very older patients (>75 years, ≈10%) undergoing AF ablation is relatively low. Nevertheless, this cohort represents the largest population treated with the PFA system to date, allowing for comparisons with their younger counterparts.

CONCLUSIONS

Drawing from these findings, using the FARAPULSE system for AF ablation in older patients (≥75 years) demonstrated swift, safe, and effective acute outcomes, mirroring a comparable pattern observed in younger patients as for the complication rate. Older patients had an arrhythmia recurrence rate consistent with findings reported in the current literature for ablation using purely thermal energy sources. Patients <65 years of age showed a markedly favorable outcome, with a significantly lower arrhythmia recurrence rate and later recurrences than older patients.

ARTICLE INFORMATION

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Supplemental Material

Figure S1

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