

Five-year efficacy of pulmonary vein antrum isolation as a primary ablation strategy for atrial fibrillation: a single-centre cohort study

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Aims

Pulmonary vein antrum isolation (PVAI) is the cornerstone of atrial fibrillation (AF) ablation. There is an ongoing discussion on whether and when to add substrate modification to PVAI. This study evaluates (1) long-term efficacy of PVAI as a primary ablation strategy in all patients independently from AF type and (2) predictors of arrhythmia recurrence.

Methods and results

A total of 509 consecutive patients (mean age 57 years, 38.9% non-paroxysmal AF) with AF underwent PVAI. In redo procedures, ablation was restricted to re-pulmonary vein (PV) isolation in case of PV reconnection. If the PVs were found to be isolated, substrate modification was performed. In total, 774 procedures were performed. Mean follow-up duration after the first and last ablation was, respectively, 66 ± 23 and 55 ± 25 months. A single PVAI was sufficient in restoring and maintaining long-term sinus rhythm in 41.3% ($n = 210$) of patients. Multiple procedures (mean 1.5) with re-PV isolation increased long-term success to 58.3% ($n = 297$). Additional substrate modification ($n = 70$) increased success to 62.5% ($n = 318$). After the last ablation, 87.5% of patients experienced success or significant clinical improvement on or off antiarrhythmic drugs. The incidence of left-sided atrial flutter or atrial tachycardia was 5% after PVAI and increased to 32% after additional substrate modification. Independent predictors for arrhythmia recurrence after the last ablation were non-paroxysmal AF, female sex, body mass index, hypertension, and AF duration.

Conclusion

Five-year freedom of atrial tachyarrhythmia could be achieved by PVAI as primary ablation strategy in 58.3% of patients. Additional substrate modification only moderately increased overall success.

Keywords

Catheter ablation • Atrial fibrillation • Pulmonary vein antrum isolation • Long-term outcome

Introduction

Atrial fibrillation (AF) is the world's most common cardiac arrhythmia. A variable substrate, triggers, and modulating factors are creating a pathogenic triangle embracing AF. Rapidly firing ectopic foci, mainly located in the pulmonary veins (PVs), can initiate AF.¹ Electrical, structural, and functional remodelling contribute to atrial substrate, which may play a role in the maintenance of AF.²

The cornerstone of catheter ablation of AF is pulmonary vein antrum isolation (PVAI).³ Blocking the 'trigger' by electrically

isolating the PVs can prevent the initiation of AF.¹ There is an ongoing discussion on whether and when to add substrate modification to PVAI, especially in (longstanding) persistent AF. Long-term follow-up studies of PVAI as a primary ablation strategy in large patient cohorts are limited.^{4–9}

We present 5-year follow-up data from a large single-centre cohort. The aim of this study was to evaluate long-term efficacy of PVAI as a primary ablation strategy in all patients independently from the type of AF. Also, predictors for arrhythmia recurrence will be assessed.

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What's new?

- Our study shows that 5-year freedom of atrial tachyarrhythmias can be achieved by pulmonary vein antrum isolation alone in 58.3% of patients suffering from atrial fibrillation (AF).
- Additional substrate modification only moderately increases overall long-term success.
- After multiple ablations, 87.5% of patients experiences success or significant clinical improvement.
- Female sex, non-paroxysmal AF, body mass index, hypertension, and history of AF before the first ablation are independent predictors of recurrence of atrial tachyarrhythmias after multiple catheter ablations.

Methods

Study population

All consecutive patients suffering from symptomatic, drug-refractory, or drug-intolerant AF who underwent primary PVAI in the University Medical Center Utrecht from 2005 to 2011 were included in this study. Baseline and long-term follow-up data of 518 patients were collected prospectively. This study was approved by the institutional review board.

Measurements

Baseline characteristics were collected prospectively and comprised age, sex, type of AF, history of AF (years since AF was diagnosed), risk factors for cardiovascular disease, the presence of structural heart disease, and left atrial (LA) size. Atrial fibrillation was classified as paroxysmal, persistent, or longstanding persistent according to the HRS/EHRA/ECAS 2012 Consensus Statement on Catheter and Surgical Ablation of AF.³ Left atrial size was assessed by echocardiography by measuring end-systolic LA diameter in the parasternal long-axis view.

Ablation protocol during the initial procedure

In all patients independently from type of AF, the primary ablation strategy was PVAI without additional linear lesions in the left atrium and/or ablation of complex fractionated atrial electrograms (CFAE). If there was a history of documented atrial flutter (AFL), ablation of the cavotricuspid isthmus was performed.

From 2005 to 2010, patients underwent magnetic resonance imaging (MRI) of the heart in a preclinical stage to define LA and PV anatomy. Transoesophageal echocardiography was performed prior to the procedure to rule out LA appendage (LAA) thrombus. From 2011, a computed tomography (CT) scan of the heart was used to assess both LA and PV anatomy and LAA thrombus before ablation.

Antiarrhythmic drugs (AADs) were discontinued five half-lives prior to ablation. An exception was made for amiodarone, which was continued due to its long half-life. At least 4 weeks of systemic anticoagulation at a therapeutic level were required before the procedure.

Electrophysiological study

Electrophysiological study has been described previously.¹⁰ In short, after trans-septal puncture, an intravenous bolus of heparin (5000 IU) was administered, followed by additional boluses to maintain an activated clotting time between 300 and 350 s. An irrigated tip catheter

(ThermoCool® irrigated tip catheter or since the end of 2013 ThermoCool® SmartTouch™, Biosense Webster) was used to widely encircle the right and left PVs at their antrum with point-by-point ablation lesions. Radiofrequency (RF) energy was delivered with a maximum power of 40 W and a maximum temperature of 43°C. Irrigation flow rate was 17 ml/min. At the posterior wall, maximum power was limited to 30 W. The endpoint of the ablation procedure was electrical isolation of all PVs as determined with a circumferential mapping catheter. Pulmonary vein isolation had to be consistent 30 min after the last RF application. Administration of adenosine to test for PV reconnection was left to operator's discretion. In case of persistence of AF, electrical cardioversion was applied to restore sinus rhythm.

Ablation protocol during repeat procedure

A repeat procedure was recommended to patients with recurrences of atrial tachyarrhythmias after a 3 months blanking period. In this procedure, PVs were checked for reconnection. In case of PV reconnection, ablation was restricted to re-PV isolation without additional substrate modification. In patients without PV reconnection, in whom electrical cardioversion failed after re-isolation or in patients with macro-re-entrant tachycardias or atrial tachycardias (ATs), additional ablation strategies were applied. Possible strategies were based on observations made during electrophysiological study and consisted of LA linear ablation of the roof (connecting both superior PVs) and the mitral isthmus (mitral annulus to the ostium of the left inferior PV), ablation of non-PV triggers [e.g. isolation of the superior vena cava (SVC)], and ablation of CFAE. If additional lines were applied, endpoint was line completeness (bidirectional block).

Post-ablation care

Oral anticoagulation was continued after ablation. Subcutaneous low-molecular-weight heparin injections were given until a therapeutic international normalized ratio was reached. All patients were treated with AADs for at least 3 months and with oral anticoagulation for at least 6 months after ablation. Three months post-ablation, patient's rhythm status and cardiac medication were assessed. If patients were free of atrial tachyarrhythmias, AADs were discontinued. Rhythm status off AADs was reassessed after 6 months. Anticoagulation therapy was individualized according to rhythm status and the CHADS₂ and CHA₂-DS₂-VASc score.

Follow-up

Patients were seen at the outpatient clinic at 3, 6, 12, and 24 months after the procedure. Rhythm status was evaluated using patient's history and a 12-lead electrocardiogram (ECG) in every visit and with additional 48-h Holter recordings at 3 and 6 months. Additional Holter recordings were left to the physician's discretion and were frequently performed in case of symptoms. Three months after ablation, MRI/CT scan was repeated to exclude PV stenosis. In early 2014, all patients and/or their referring physicians were contacted to assess for recurrence of symptoms and rhythm documentation. Patients who did not respond or who could not be reached were considered lost to follow-up and excluded from the study.

Outcomes

Possible long-term outcomes were success, clinical success, or failure. Long-term success was defined as freedom from atrial tachyarrhythmia recurrences following the 3-month blanking period through a minimum of 36 months of follow-up from the date of the ablation procedure in the absence of Class I and III AAD therapy. Recurrence is defined as the

occurrence of AF, AFL, or AT of at least 30 s duration, documented by an ECG or device recording system.³

Long-term clinical success was defined as a significant reduction in the number of AF episodes, the duration of AF episodes, or the % time a patient is in AF in the presence or absence of previously ineffective AAD therapy. Clinical success on top of success is referred to as combined success.

Statistical analysis

Patient characteristics were reported as percentages, counts, or mean \pm standard deviation (SD), as appropriate. Differences in categorical variables between groups were compared by the χ^2 test.

The follow-up period was calculated from the date of the procedure to that of the outcome event (atrial tachyarrhythmia recurrence) or censoring (end of follow-up and death) events. The estimated event-free survival probabilities were calculated using the Kaplan–Meier analysis.

Multivariate Cox regression was used to identify significant predictors of AF recurrence after the first and last procedure. Based on known or expected clinical relevance, predictors were selected for the multivariate prediction models. All potential predictors were entered into the model, regardless of their statistical significance in univariate analysis. Multivariable Cox regression models assume that continuous variables relate linearly to the response. Restrictive cubic splines were used to detect non-linear associations between continuous predictors and the outcome. The discriminative ability of the Cox models was evaluated with Harrell's concordance statistics (c-statistic).

A *P*-value of < 0.05 was considered statistical significant. Statistical analyses were performed using SPSS 21.0 (IBM, Armonk, NY, USA).

Results

Of 518 consecutive patients, 9 (1.7%) could not be reached for the assessment of arrhythmia recurrence and were excluded from this study. Patient characteristics are shown in *Table 1*.

Three hundred and eleven patients (61.1%) suffered from paroxysmal atrial fibrillation (PAF). Of the 198 patients with non-PAF, 130 (25.5% of the total population) had persistent AF and 68 (13.4% of the total population) had longstanding persistent AF.

A total of 774 procedures were performed, with a mean of 1.5 per patient. Three hundred and one patients had 1 and 208 had multiple procedures, of which 160 had 2, 39 had 3, and 9 had 4 ablations.

Mean procedure duration from femoral vein access to catheter withdrawal was 248 ± 76 min, and mean fluoroscopy time was 39.3 ± 18.8 min. Complications occurred in 6.8% of procedures (*Table 2*). One patient (0.1%) died suddenly 5 weeks after the procedure. Autopsy revealed a peri-epicarditis with significant pericardial effusion. During follow-up, another 22 patients died. These deaths were not related to catheter ablation, with cancer being the leading cause of death.

Outcomes after a single pulmonary vein antrum isolation

During the first procedure, successful electrical isolation of all PVs could be achieved in 99.4% of patients. During a mean follow-up of 66 ± 23 months (5.5 years), a single PVAI without additional substrate modification was sufficient in restoring and maintaining long-term sinus rhythm in 41.3% ($n = 210$) of patients. Long-term success was significantly greater in PAF (48.6%) compared with

Table 1 Baseline characteristics

Demographics ($n = 509$)	
Male sex	386 (75.8%)
Age at first ablation, years	57 ± 9.7
PAF	311 (61.1%)
Persistent AF	130 (25.5%)
Longstanding persistent AF	68 (13.4%)
History of AF, years	6.9 ± 6.1
BMI, kg/m ²	27 ± 4.3
Hypertension	168 (33.0%)
Diabetes mellitus	29 (5.7%)
Hypercholesterolemia	111 (21.8%)
Atrial flutter	140 (27.5%)
Structural heart disease	
Ischaemic	41 (8.1%)
Valvular	10 (2.0%)
HCM	8 (1.6%)
DCM	3 (0.6%)
AVRC	1 (0.2%)
Non-compaction	1 (0.2%)
Congestive heart failure	28 (5.5%)
Lone AF	117 (23.0%)
CHA ₂ DS ₂ -VASc score	1.1 ± 1.2
LA size, mm	43.1 ± 6.1

Data are expressed as mean \pm SD or as number (percentage).

AF, atrial fibrillation; BMI, body mass index; HCM, hypertrophic cardiomyopathy; DCM, dilated cardiomyopathy; AVRC, arrhythmogenic right ventricular cardiomyopathy; LA, left atrium.

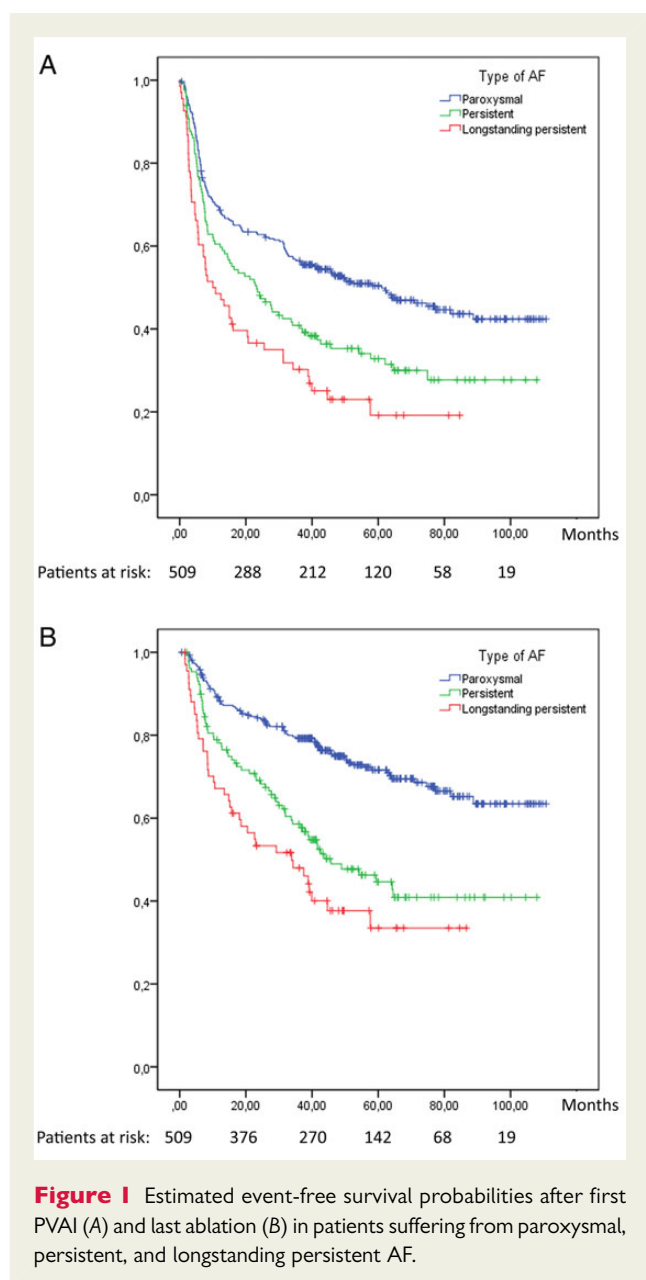
Table 2 Complications in 774 procedures

Complication	N (%)
Vascular complications	17 (2.2)
Significant PV stenosis of $>50\%$	16 (2.1)
Pericarditis	2 (0.3)
Pericardial effusion	11 (1.4)
Leading to tamponade requiring pericardiocentesis	10 (1.3)
Stroke	1 (0.1)
TIA	2 (0.3)
Anaphylactic reaction on medication	2 (0.3)
Myocardial infarction	1 (0.1)
Death	1 (0.1)

TIA, transient ischaemic attack.

persistent (33.1%) and longstanding persistent AF (23.5%), as shown in *Figure 1A* (significance was found pairwise in all groups).

Most recurrences (61%) occurred within 12 months after ablation, although late recurrences >3 years after ablation were seen in 14%. Predictors of AF recurrence are shown in *Table 3*. After a single procedure, persistent AF [hazard ratio (HR): 1.52, 95% confidence interval (CI): 1.16–1.99], longstanding persistent AF (HR:



2.01, 95% CI: 1.44–2.80), and history of AF (HR: 1.02, 95% CI: 1.01–1.04) independently predicted arrhythmia recurrences. The c-statistic was 0.59.

Outcomes after one or multiple procedures

Out of the total patient group of 509 patients, 58.7% ($n = 299$) experienced recurrence of atrial tachyarrhythmias after the first procedure and 40.9% ($n = 208$) underwent at least one repeat procedure. That implies that 91 out of 299 patients (30%) with arrhythmia recurrence after the first ablation chose not to undergo a redo procedure.

During a mean follow-up of 55 ± 25 months (4.5 years) after the last procedure, total success after multiple procedures was 62.5%

($n = 318$): 72.3% in PAF, 50.0% in persistent AF, and 41.2% in longstanding persistent AF (Figure 1B).

Pulmonary vein antrum isolation alone

As reported above, a single PVAI without additional substrate modification restored and maintained long-term sinus rhythm in 41.3% ($n = 210$) of patients. Repeated PVAIs without additional ablations increased success to 58.3% ($n = 297$) in the total group of 509 patients: PAF: 67.8%, persistent AF: 46.2%, and longstanding persistent AF: 38.2% (Table 4). That means that of the 318 patients with successful ablation, PVAI alone was performed in 93.4% (PAF: 92.3%, persistent AF: 93.8%, longstanding persistent: 92.9%).

At the second procedure, reconnection of the PVs was present in 89.4% of patients and re-PV isolation was performed. Pulmonary vein reconnection at the start of the first redo procedure was more often found in PAF (93.6%) compared with non-PAF (persistent AF 86.4%, longstanding persistent AF 82.1%). Pulmonary vein reconnection was found in 58.3% of patients during the third and in 33.3% of patients during the fourth procedure (Table 5).

Additional ablation strategies

Additional ablation strategies were applied in 70 patients and in 34% of all redo procedures. In 30% ($n = 21$) of these 70 patients, long-term sinus rhythm was successfully restored and maintained. In the total patient group of 509 patients, additional substrate modification increased success to 62.5% ($n = 318$). Thus, additional ablation added 4.2% to total long-term success. All additional strategies were more often used in non-PAF patients (PAF: 22.2% vs. persistent AF: 39% vs. longstanding persistent AF: 54.7%), although it led to significantly higher long-term success in PAF (53.8 vs. 20.8 vs. 10% $P = 0.003$).

Linear LA ablation was performed in 26% of redo procedures: roofline between the superior PVs in 21.6%, LA-isthmus line between the left inferior PV, and the mitral annulus in 12.9%. Complex fractionated atrial electrograms ablation was performed in 16.7% of redo procedures. In 2.7% of redo procedures, a non-PV trigger was found in the SVC with subsequent isolation of the SVC (Table 5).

Clinical success

After the last procedures, long-term clinical success, as defined above, was found in 25% of 509 patients ($n = 127$). Of these patients, 66.9% were still on AAD therapy. That means that combined success (success and/or clinical success) could be achieved in 87.5% of the total patient group (PAF: 92.6%, persistent AF: 84.6%, longstanding persistent AF: 69.1%, Table 4). Finally, in 12.6% of 509 patients ($n = 64$), one or multiple catheter ablation procedures resulted in failure (PAF: 7.4% vs. persistent AF: 15.4% vs. longstanding persistent AF: 30.9%). An overview of results is shown in Figure 2.

Left atrial tachyarrhythmias

After one or multiple PVAIs without additional substrate modification or linear ablation, most recurrences were based on AF (90.3%). Right-sided AFL occurred in 14 patients (4.7%). Fifteen patients (5%) experienced left-sided atrial macro-re-entry tachycardia ($n = 12$) or focal left-sided AT ($n = 3$). After substrate modification, recurrences were based on left-sided atrial macro-re-entry tachycardia

Table 3 Predictors of recurrence of atrial tachyarrhythmia after a single PVAI and after the last ablation

Predictors	After a single PVAI			After the last ablation		
	Multivariate HR	95% CI	P-value	Multivariate HR	95% CI	P-value
Female sex	1.30	0.98–1.71	0.065	1.47	1.04–2.08	0.029
Age at first ablation, years	1.00	0.99–1.02	0.822	1.00	0.99–1.02	0.307
Persistent AF	1.52	1.16–1.99	0.000	2.19	1.56–3.06	0.000
Longstanding Persistent AF	2.01	1.44–2.80	0.000	2.94	1.96–4.39	0.000
History of AF, years	1.02	1.01–1.04	0.019	1.03	1.01–1.05	0.001
BMI	0.99	0.96–1.02	0.480	0.98	0.95–1.02	0.403
BMI ²	^a	^a	^a	1.02	1.01–1.03	0.006
Hypertension	1.20	0.92–1.56	0.175	1.57	1.13–2.18	0.007
Diabetes mellitus	0.73	0.41–1.31	0.734	0.63	0.29–1.37	0.243
Hypercholesterolemia	1.04	0.77–1.40	0.807	0.84	0.56–1.26	0.394
Structural heart disease						
Ischaemic	0.83	0.52–1.31	0.417	0.94	0.53–1.69	0.846
Lone AF	1.01	0.71–1.45	0.938	1.22	0.78–1.92	0.376
LA size, mm	1.02	0.99–1.04	0.072	1.02	0.99–1.04	0.179

Bold values are considered statistical significant (P values <0.05).

HR, Hazard ratio; CI, confidence interval; BMI², because of the parabolic response of BMI after the last ablation, square BMI is used.

^aNot included in the model.

Table 4 Results after a single PVAI, multiple re-PV isolations, and substrate modification in patients suffering from paroxysmal, persistent, and longstanding persistent AF

	PAF (n = 311) (%)	Persistent AF (n = 130) (%)	Longstanding persistent AF (n = 68) (%)	Total (n = 509) (%)
Success after single PVAI	48.6	33.1	23.5	41.3
Success after multiple re-PV isolations	67.8	46.2	38.2	58.3
Total success including substrate modification	72.3	50.0	41.2	62.5
Combined success after the last procedure ^a	92.6	84.6	69.1	87.5

^aSuccess + clinical success.

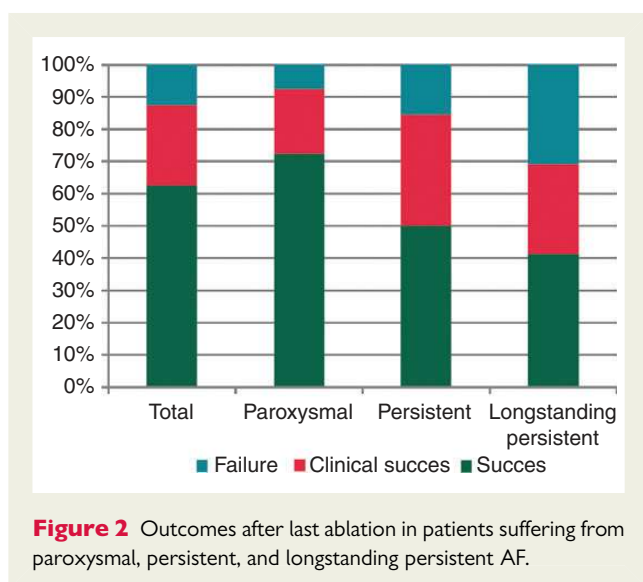
Table 5 Redo procedure characteristics

	Second procedure (n = 208) (%)	Third procedure (n = 48) (%)	Fourth procedure (n = 9) (%)	All redo procedures (n = 265) (%)
PAF	52.9	41.7	33.3	50.9
PV reconnection ^a	89.4	58.3	33.3	81.9
Additional ablations ^b	25.5	58.3	88.9	33.6
Ablation of CFAE	10.6	33.3	44.4	15.8
Roofline	16.8	33.3	66.7	21.5
LA isthmus	10.1	18.8	44.4	12.8
SVC isolation	1.9	6.3	0	2.6

^aMost reconnection occurred in the RIPV.

^bMultiple additional ablations could be applied in a single patient.

CFAE, complex fractionated electrograms; LA, left atrium; SVC, superior vena cava.



in 10% of patients and on focal left-sided AT (micro-re-entry) in 22% of patients.

Predictors of atrial fibrillation recurrence after the last ablation

Cubic spline functions showed a non-linear association of body mass index (BMI) with the outcome, resembling a parabolic form. For ease of interpretation, we therefore added BMI squared to the Cox regression model. Female sex (HR: 1.47, 95% CI: 1.04–2.08), persistent AF (HR: 2.19, 95% CI: 1.56–3.06), longstanding persistent AF (HR: 2.94, 95% CI: 1.96–4.39), history of AF (HR: 1.03, 95% CI: 1.01–1.05), BMI² (HR: 1.02, 95% CI: 1.01–1.03), and hypertension (HR: 1.57, 95% CI: 1.13–2.18) independently predicted arrhythmia recurrence after the last ablation procedure (Table 3).

The c-statistic was 0.68.

Discussion

Main findings

Our study showed that 5-year freedom of atrial tachyarrhythmias could be achieved by PVAI as a primary ablation strategy in 58.3% of patients suffering from AF, although 40.9% of patients underwent multiple procedures. Thirty per cent ($n = 91$) of patients with recurrence of atrial tachyarrhythmias after the first ablation chose not to undergo a redo procedure. Therefore, success of PVAI after multiple procedures may be underestimated.

Success was highest in patients with PAF (67.8%) and decreased to 38.2% in patients with longstanding persistent AF. Additional and sometimes extensive substrate modification was performed in 34% of all redo procedures but added only 4.2% to total long-term success (62.5%). Another 25% of patients showed significant clinical improvement, which implies that combined success was achieved in 87.5% of patients. Left-sided atrial macro-re-entry and AT were an uncommon finding after PVAI alone (5%), but their incidence increased to 32% after additional substrate modification. These results support the importance of PVAI even in patients with

persistent and longstanding persistent AF, and emphasize that the role of additional substrate modification is still controversial.

Predictors for arrhythmia recurrence after the last ablation were non-PAF, history of AF, female sex, hypertension, and BMI. The complication rate is comparable with previous studies.¹¹

Previous studies focusing on pulmonary vein antrum isolation as a primary ablation strategy

Previous studies with PVAI as a primary ablation strategy showed 29–57% long-term success after one ablation in PAF.^{4,5,7–9} Medi et al. ($n = 100$) and Gaita et al. ($n = 41$) showed that multiple re-PV isolations without additional ablations increased success to 57 and 62%, respectively.^{5,8}

Two studies described long-term follow-up after PVAI as a primary ablation strategy in non-PAF. Tiltz et al. included 202 patients suffering from longstanding persistent AF. After a median follow-up of 56 months, multiple PV isolations established long-term sinus rhythm in 24.3% of patients.⁶ In a small study of 26 patients with (longstanding) persistent AF, Gaita et al. reported a 3-year success of 39% after multiple PV isolations.⁸

Second-generation cryoballoon ablation has shown comparable results in PAF patients. Only recently, cryoballoon ablation was studied in patients with persistent AF. After a single procedure, reported clinical success after 12 months was up to 69%.¹² No randomized controlled trials have yet been performed comparing RF ablation with cryoballoon ablation.

Additional substrate modification

In our study, patients with non-PAF showed higher recurrence rates compared with patients with PAF after PVAI alone. Moreover, at redo procedures, isolated PVs were more often found in the non-PAF group. These findings support the hypothesis that an atrial substrate has a greater role in the initiation and maintenance of AF in non-PAF patients. Nevertheless, additional substrate modification only moderately increased success rates.

Recently, two multicentre randomized controlled trials compared the efficacy of adding substrate modification with PVAI in non-PAF patients. The STAR-AF II trial ($n = 589$) compared the efficacy of three different primary ablation strategies in patients with (longstanding) persistent AF. After 18 months of follow-up, no benefit was found in AF reduction when additional substrate ablation (CFAE or lines) was performed on top of PVAI.¹³ The RADAR-AF trial ($n = 117$, follow-up of 12 months) showed no differences in success rates between PVAI alone vs. PVAI and ablation of high-frequency sources; ‘drivers’ in patients with persistent AF.¹⁴

A different ablation strategy in non-PAF patients is the ‘stepwise approach’. After PVAI, extensive substrate modification is performed with termination of AF as a procedural endpoint.¹⁵ Recently, two cohort studies revealed 5-year follow-up data of the ‘stepwise approach’ in (longstanding) persistent AF patients.^{16,17} Fairly large differences in success off AADs after multiple ablations (mean of 2.1 in both studies) were found. Schreiber et al. ($n = 489$) showed 46% success, whereas 64.7% of the patients in the study of Scherr et al. ($n = 150$) were free of arrhythmia recurrence. No randomized

trials comparing the stepwise approach and PVAI as a primary ablation strategy are performed yet.

Predictors for arrhythmia recurrence

Predictors for recurrence after both the first and last ablation were non-PAF and history of AF. Female sex, hypertension, and BMI were additional independent predictors for recurrence after the last ablation. A meta-analysis of 13 studies showed similar independent predictors: non-PAF (seven studies), female sex (four studies), hypertension (three studies), and BMI (one study). Two other predictors were age (four studies) and LA size (three studies).¹⁸ These two factors did not predict AF recurrence in our patient group. We assessed LA size on echocardiography by measuring end-systolic LA diameter in the parasternal long-axis view, but recent reports showed that this parameter correlates poorly with true LA volume.¹⁹

After the first ablation, recurrence is not well predictable (Harrell's C: 0.59). This might be due to the arbitrariness in PV reconnection, which diminishes after multiple procedures.

Clinical implications

The definition of long-term success is strict; patients must be free of atrial tachyarrhythmias for at least 36 months off AAD therapy.³ Although this strict definition is essential in comparing outcomes of different ablation strategies in clinical research, it does not fully represent the patient's perspective on the treatment. In spite of (infrequent) arrhythmia recurrences, patients often experience significant clinical improvement and describe the treatment as successful. Therefore, clinical success (on top of success) is an important outcome. Our study showed that combined success was 87.5% in the total population. Thus, PVAI can eliminate AF or can significantly improve clinical complaints, reduce the number or duration of AF episodes, or the need of AAD therapy in most patients. The particular strength of this study is that these results are achieved with a consistent primary ablation strategy; PVAI without additional substrate modification. If substrate modification would have been part of the primary ablation strategy, a large number of patients—particularly patients with PAF, but also with persistent and longstanding persistent AF—would have received unnecessary extensive ablations. More extensive ablation strategies have the risk of inducing regular left-sided AFL or AT in up to 40% of patients.¹⁵ These tachycardias are often more difficult to treat by catheter ablation than the initial arrhythmia. In our study, only 5% of recurrences after PVAI were based on left-sided AFL or AT. These results are comparable with previous studies.²⁰ Yet, long-term outcomes after PVAI alone especially in longstanding persistent AF remain moderate, and the optimal ablation strategy in this subset of patients is still waiting to be defined. Routine contact force and adenosine-guided PVAI may increase success and avoid repeated ablation procedures.

Potential limitations

(1) This is a single-centre non-randomized report with the associated limitations of this study design. However, we had no selection bias because all consecutive patients undergoing primary PVAI for AF at our centre were included for analysis.

- (2) During this study, technical developments may have influenced the results (i.e. the introduction of contact force ablation catheters during the last months of the study and the limited use of adenosine in early years of the study).
- (3) Duration and intensity of arrhythmia monitoring influence the likelihood of detection of AF during follow-up. Our follow-up was based on clinical evaluation and 48-h Holter ECG recordings. Some paroxysmal asymptomatic episodes of AF may have been missed.

Conclusion

Five-year freedom of atrial tachyarrhythmias off AADs could be achieved by PVAI alone in 58.3% of patients suffering from AF. Additional substrate modification only moderately increased overall long-term success. After the last ablation, 87.5% of patients experienced success or significant clinical improvement. During follow-up, the incidence of left-sided AFL and AT was 5% after PVAI alone, but increased to 32% after additional substrate modification. Female sex, non-PAF, BMI, hypertension, and history of AF before the first ablation were independent predictors of recurrence of atrial tachyarrhythmias after multiple catheter ablations.

Conflict of interest: None declared.

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High-density biatrial activation mapping during typical atrial flutter after bicavopulmonary bypass

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A 35-year-old man with a complex univentricular congenital heart disease (double inlet left ventricle with levo-transposition of the great arteries) was referred for recurrent atrial tachycardia. He underwent Fontan surgical procedure at age 8 and total cavopulmonary connection at age 22 with an intra-cardiac unfenestred tube together with a septostomy and a right Maze procedure.

He manifested with recurrent right atrial tachycardia for 13 years despite antiarrhythmic drugs.

The Rhythmia™ system (Boston Scientific) was used for mapping.¹ Access to the atrial bulge was performed through retrograde aortic route, passing through the single ventricle then retrogradely crossing the mitral annulus then through the atrial septal defect, allowing mapping around the intra-cardiac tube and reaching the most lateral part of the right atrium. The activation reference catheter was placed inside the intra-cardiac tube by venous femoral access.

Mapping was performed in 32 min (28 669 activation points), revealing a counterclockwise typical atrial flutter (Figure). Positioning the ablation catheter on the cavotricuspid isthmus and delivering a 30 W irrigated radio-frequency application led to termination of the tachycardia. The whole procedure duration was 210 min with 54 min fluoroscopy. The patient did not complain of any recurrence over the following 3 months.

The full-length version of this report can be viewed at: <http://www.escardio.org/Guidelines-&-Education/E-learning/Clinical-cases/Electrophysiology/EP-Case-Reports>.

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