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Five-Year Outcome of Catheter Ablation of Persistent Atrial Fibrillation Using Termination of Atrial Fibrillation as a Procedural Endpoint

Running title: *Scherr et al.; Five-Year Outcome of Persistent AF Ablation*

Daniel Scherr, MD[1,2]; Paul Khairy, MD, PhD[1]; Shinsuke Miyazaki, MD[1]; Valerie Aurillac-Lavignolle, BSc[1]; Patrizio Pascale, MD[1]; Stephen B. Wilton, MD[1]; Khaled Ramoul, MD[1]; Yuki Komatsu, MD[1]; Laurent Roten, MD[1]; Amir Jadidi, MD[1]; Nick Linton, MD, PhD[1]; Michala Pedersen, MD[1]; Matthew Daly, MD[1]; Mark O'Neill, MD[1]; Sebastien Knecht, MD, PhD[1]; Rukshen Weerasooriya, MD[1]; Thomas Rostock, MD[1]; Martin Manninger, MD[2]; Hubert Cochet, MD[1] Ashok J. Shah, MD[1]; Sunthareth Yeim, MD[1]; Arnaud Denis, MD[1]; Nicolas Derval, MD[1]; Meleze Hocini, MD[1]; Frederic Sacher, MD[1]; Michel Haissaguerre, MD[1]; Pierre Jais, MD[1]

[1]Hôpital Cardiologique du Haut Lévêque, Université Victor-Segalen Bordeaux, Pessac, France; [2]Division of Cardiology, Department of Medicine, Medical University of Graz, Austria

Correspondence:
Daniel Scherr, MD
Division of Cardiology
Medical University of Graz
Auenbruggerplatz 15
8036 Graz, Austria
Tel: +4331638512544
Fax: +4331638513733
E-mail: daniel.scherr@medunigraz.at

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Abstract

Background - This study aimed to determine five-year efficacy of catheter ablation for persistent atrial fibrillation (PsAF) using AF termination as a procedural endpoint.

Methods and Results - 150 patients (57±10 years) underwent PsAF ablation using a stepwise ablation approach (pulmonary vein isolation, electrogram-guided and linear ablation) with the desired procedural endpoint being AF termination. Repeat ablation was performed for recurrent AF or atrial tachycardia (AT). AF was terminated by ablation in 120 patients (80%). Arrhythmia-free survival rates after a single procedure were 35.3±3.9%, 28.0±3.7%, and 16.8±3.2% at 1, 2, and 5 years, respectively. Arrhythmia-free survival rates after the last procedure (mean 2.1±1.0 procedures) were 89.7±2.5%, 79.8±3.4%, and 62.9±4.5%, at 1, 2, and 5 years, respectively. During a median follow-up of 58 (IQR 43-73) months following the last ablation procedure, 97 of 150 (64.7%) patients remained in sinus rhythm without antiarrhythmic drugs (AADs). Another 14 (9.3%) patients maintained sinus rhythm after re-initiation of AADs, and an additional 15 (10.0%) patients regressed to paroxysmal recurrences only. Failure to terminate AF during the index procedure (HR 3.831; 95%CI: 2.070-7.143; p<0.001), left atrial diameter ≥50mm (HR 2.083; 95%CI: 1.078-4.016; p=0.03), continuous AF duration ≥18 months (HR 1.984; 95%CI: 1.024-3.846; p<0.04) and structural heart disease (HR 1.874; 95% CI: 1.037-3.388; p=0.04) predicted arrhythmia recurrence.

Conclusions - In patients with PsAF, an ablation strategy aiming at AF termination is associated with freedom from arrhythmia recurrence in the majority of patients over a 5-year follow up period.Procedural AF non-termination and specific baseline factors predict long-term outcome after ablation.

Key words: ablation; atrial fibrillation; atrial tachycardia

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Introduction

Catheter ablation is an established treatment option for patients with symptomatic drug refractory AF.[1] In paroxysmal AF (PAF) ablation, pulmonary vein isolation (PVI) alone is a well-defined procedural endpoint.[1-3] This strategy, although effective in maintaining sinus rhythm (SR) for PAF,[3] has limited success in persistent AF (PsAF).[1,4-7] The understanding of the substrate maintaining persistent AF remains rudimentary. The targets and endpoints of PsAF ablation are ill-defined, and there is no consensus on the optimal ablation strategy in these patients. Whether termination of AF by ablation is associated with a lower risk of recurrent arrhythmia compared to procedural failure to terminate AF with the need for electrical cardioversion remains controversial.[8-19]

Finally, data on long-term outcome of PsAF ablation ≥5 years is limited,[6-20] and the predictors of arrhythmia recurrence after PsAF ablation are ill-defined.

The aims of this prospective observational study were twofold: 1) to determine the five-year outcome in PsAF patients who underwent a stepwise ablation approach aiming at procedural AF termination and 2) to determine whether procedural AF termination and other baseline factors impact arrhythmia recurrence during long-term follow-up.

Methods

Study Population

The study population comprised 150 consecutive patients undergoing their first catheter ablation for persistent AF between November 2003 and October 2007 at our institution. Persistent AF was defined as continuous AF sustained beyond seven days. [1,21] Longstanding persistent AF was defined as persistent AF >12 months' duration.[1,21] As for inclusion criteria, a total AF history ≥6 months and a continuous AF duration ≥1 month were required. All patients had failed to

maintain SR despite cardioversion and/or treatment with ≥1 AAD. Only patients who presented for the ablation procedure in AF were included. Baseline characteristics are summarized in Table 1. This study was approved by the institutional review committee of the University of Bordeaux Health System, and all patients gave written informed consent.

Electrophysiological Study and Ablation Procedure

Details of the peri-procedural management and the ablation technique at our institution have been described previously,[8,9,11,12,21-24] and are described in detail in the online data supplement. As it is standard clinical practice at our institution, all AADs were discontinued at least five half-lives prior to ablation except for amiodarone (n=32). All patients received oral anticoagulation (target INR 2–3) for at least 1 month prior to the procedure. Patients underwent transesophageal echocardiography within 48 h of the procedure to rule-out atrial thrombus. Warfarin was restarted the day after the procedure for at least six months after each ablation procedure and was continued thereafter at the physician's discretion.

In all patients, sequential stepwise ablation was performed in the following order: PVI, electrogram-based ablation, and linear ablation.

Circumferential PVI was performed with the endpoint of abolition or dissociation of electrical activity of all PVs. When AF did not terminate during PVI, the procedure was continued with electrogram-based ablation in the LA. When electrogram-based ablation of the LA did not result in organization of the coronary sinus, additional ablation within the coronary sinus was performed. Linear ablation was performed if AF persisted following the previous ablation steps. A roof line was performed joining the right and left superior PVs, and if AF continued, a mitral isthmus line from the mitral annulus to the left inferior PV was performed, with the endpoint of abolition of local electrograms.

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Electrogram-based ablation was continued in the right atrium (RA) if AF did not terminate during LA ablation and the RA appendage demonstrated a shorter cycle length than the LA appendage. Linear ablation was performed in all patients at the cavotricuspid isthmus either before or after restoration of SR and bidirectional conduction block was confirmed.

Procedural Endpoints

The primary procedural endpoint was termination of AF, which was defined as a transition directly from AF to SR or from AF to one or more ATs without antiarrhythmic drugs or electrical cardioversion. Whenever AF terminated to one or more ATs these were targeted for ablation until SR was achieved. When SR had not been restored by ablation, the AT was terminated by cardioversion. When AF was not terminated by ablation, SR was restored by cardioversion. Once SR was achieved, verification of entrance block of all PVs, and bidirectional block along all linear ablations was checked and, if necessary, supplemental ablation was performed as required to achieve block. No attempt at arrhythmia reinduction was made.

Repeat procedures were performed targeting the documented recurrent arrhythmia and following the same stepwise approach aiming at arrhythmia termination.

Follow Up

Patients were followed up at our institution 1, 3, 6, and 12 months post-procedure, and every 6 months thereafter, including 24h Holter monitoring. When patients had been asymptomatic and in SR for 12 months, they were followed up at our institution at 6 monthly intervals, including 24h Holter monitoring. Patients referred from distant regions (n=12) were medically released 12 months after each procedure for regular follow-up with their local cardiologists as described, and every effort was made to update our clinical records with their progress and bi-annual Holter reports. Between visits, all patients were encouraged to seek ECGs or Holter monitoring for any

symptoms suggestive of AF. The completeness rates for Holter monitoring were 96%, 91%, 90%, 85%, 83%, 79%, and 91% at 1, 2, 3, 4, 5, 6, and 7 years, respectively. Patients were personally contacted for a final follow-up between October 2011 and May 2012, and 7-day Holter monitoring (AFT-1000, Holter Supplies, France) was performed after this visit. The overall Holter completeness rate throughout the study was 89.7%.

AADs were continued for 1–3 months following the ablation procedure. Repeat ablation was offered to patients with arrhythmia recurrence following the initial 3-month follow-up period. The primary study end point was freedom from any asymptomatic or symptomatic atrial tachyarrhythmia lasting >30 s off antiarrhythmic drugs after the last ablation procedure. Regression of PsAF was defined as change to PAF or maintenance of SR on AADs.

Statistical Analysis

Continuous variables are presented as mean±SD, or median and interquartile range (IQR,25th-75th percentiles). Categorical variables are presented as percentages (%) and counts. Two-group comparisons (i.e., with or without AF termination during ablation; with and without amiodarone at the time of procedure) of continuous variables were performed by Student t tests if normally distributed or with Wilcoxon Rank-Sum tests if the normality assumption was violated according to Shapiro-Wilk tests or visual inspection of normal probability plots. Categorical variables were compared by Chi-square tests. Baseline (i.e., variables listed in Table 1) and procedural factors (i.e., method of AF termination, procedural duration, and RF duration) associated with arrhythmia recurrence during following-up were assessed in univariate and multivariable Cox proportional hazard models, from which hazard ratios (HR) and 95% confidence intervals (CI) were derived, after verification of proportional-hazards assumption by time-dependent interactions and goodness-of-fit statistics (weighted Schoenfeld residuals). Factors associated

with P-values <0.1 in univariate analyses were included in stepwise multivariate Cox regression models. A receiver-operator characteristic (ROC) curve analysis was performed to determine the best cut-off value for the left atrial diameter and for continuous AF duration in predicting arrhythmia recurrence following the last ablation procedure. The value with the greatest discriminatory potential was selected on the basis of Youden's Index. Time to first arrhythmia recurrence was calculated and plotted using the Kaplan Meier product-limit method with comparisons performed by log-rank statistics. Two-tailed P-values <0.05 were considered to indicate statistical significance. Baseline characteristics including age, sex, co-morbidities, and pharmacological therapy were complete in all patients. Echocardiographic data were complete in 94%. Missing data were handled by listwise deletion (i.e., complete case analyses). Statistical analyses were performed using SPSS 20.0 (IBM, Armonk, New York, USA).

Results

Index Procedural Data

In 30 of 150 patients (20%) AF required pharmacological and/or DC cardioversion. (Figure 1) Of the 120 patients (80%) in whom AF terminated during ablation, 90 terminated via an intermediate step of AT and the remaining 30 converted directly from AF to SR. In those who terminated AF via AT, 75 patients could be successfully ablated to SR, whereas the remaining 15 patients required pharmacological and/or DC cardioversion to reach SR. A total number of 164ATs (1.1±1.1 ATs per patient overall) occurred.

Compared to patients without AF termination, patients with AF termination had a shorter duration of continuous AF (12 (6-19) months vs. 24 (17-44) months; p<0.001) and a smaller LA diameter (47±7 mm vs. 52±8 mm; p<0.01).

The rate of AF termination was similar in patients with and without amiodarone at the

time of the procedure (75% versus 81%, P=0.58). Mean procedural and RF durations for patients in whom termination of AF was achieved vs. not achieved were 264±74 min vs. 263±64 min (p=0.91), and 89±28 min vs. 99±27 min (p=0.09), respectively.

Single Procedure Outcome

During a median follow-up of 70 (IQR 60-81) months from the first ablation procedure until the last follow-up visit, SR was maintained in 23 of 150 (15.3%) patients following a single procedure. Arrhythmia-free survival rates after a single catheter ablation procedure were 35.3±3.9%, 28.0±3.7%, and 16.8±3.2% at 1, 2, and 5 years, respectively (see online data supplement). Arrhythmia recurred in 30 (20.0%) patients who had maintained SR for ≥1 year, including 14 (9.3%) patients with recurrences >3 years after ablation. Recurrent arrhythmias after the index procedure werePsAF in 42 (33.1%) patients, PAF in 17 (13.5%) patients, and AT in 68 (53.5%) of 127 patients.

In multivariate analysis, the only factor independently associated with arrhythmia recurrence was failure to terminate AF during the index procedure (HR 1.650; 95%CI: 1.086-2.513; p=0.02; Figure 2).

Multiple Procedure Outcome

109 patients (72.7%) underwent 167 repeat procedures (61 (36.5%) for AF, 106 (63.5%) for AT; Figure 3). Recovered PV conduction was found in 96/109 (88.1%) patients. Overall, PVI was performed in all 150 patients but was never the sole ablative strategy performed over the course of the study.

A total of 317 procedures were performed in 150 patients (2.1±1.0; median 2 (IQR 1-3)). 41 (27.3%) patients had 1 procedure, 66 (44%) had 2, 31 (20.7%) had 3, 10 (6.7%) had 4, 1 (0.7%) had 5, and 1 (0.7%) patient had 6 procedures. The first and the last redo procedures were

performed 11±13 and 19±19 months after the index procedure, respectively. During a median follow-up of 58 (IQR43-73) months following the last ablation procedure, 97/150 (64.7%) patients remained in SR without AADs, and 111 patients (74%) remained in SR when including those on AADs (Amiodarone in 6 patients).Arrhythmia-free survival rates after the last catheter ablation procedure and off AADs were 89.7±2.5%, 79.8±3.4%, and 62.9±4.5%, at 1, 2, and 5 years of follow-up, respectively (Figure 4), corresponding to an average actuarial recurrence rate of 8.5% per year. Event-free survival rates on or off AADs were 91.1±2.4%, 83.0±3.2%, and 70.4±4.2% at 1, 2, and 5 years of follow-up, respectively. Regression of AF was noted in 29 (19.3%) patients: 14 (9.3%) patients maintained SR after re-initiation of AADs, and 15 (10.0%) patients presented only with paroxysmal recurrences.

Factors associated with recurrent arrhythmias off AADs following the last ablation procedure are listed in Table 2. In multivariate analysis, independent predictors of recurrent arrhythmias were failure to terminate AF by ablation during the index procedure, structural heart disease, continuous AF duration ≥18months, and an LA diameter ≥50mm (Table 3). Freedom from recurrent arrhythmias did not differ according to whether AF was terminated in the RA or LA (p=0.83). Although the multiple-procedure success rate off AADs was lower in patients with long-standing persistent compared to persistent AF (55.1±5.6% vs. 77.8±6.8%; p=0.01; Figure 5A), lack of AF termination during ablation was associated with a higher recurrence rate independent of whether AF was persistent or long-standing persistent (HR 3.831; 95%CI: 2.070-7.143; p<0.0001).

Arrhythmia-free survival rates after multiple procedures on or off AADs did not differ between patients who terminated to directly SR vs. to AT (83.1±7.8% vs. 80.0±4.8%; p=0.92), but were significantly reduced for patients in whom ablation failed to terminate AF (29.3±9.8%;

p<0.0001; Figure 5B).

Complications

Complications occurred in 4.4% of procedures (Pericardial effusion requiring intervention (n=6), phrenic nerve injury (n=3; full recovery during follow up), major femoral hematoma requiring intervention (n=2), cerebrovascular stroke (n=1; full recovery during follow up), myocardial infarction (n=1), and LA appendage isolation (n=1; no stroke during follow up)). There were no procedure-related deaths. Three deaths occurred over the course of follow-up (skin cancer (n=1); GI cancer (n=1); postoperative death after mitral valve replacement (n=1)).

During long-term follow-up, four patients suffered an ischemic stroke. Two of these patients had previously failed AF ablation and were on warfarin with sub-therapeutic INR levels at the time of stroke and had CHA_2DS_2VAScscores of 2 and 3, respectively. The third patient had previously failed AF ablation and was on therapeutic warfarin, with a CHA_2DS_2VASc score of 4. The fourth patient had been in SR during follow-up and was off warfarin, with a CHA_2DS_2VASc score of 0. AF was documented during the hospitalization for stroke 49 months after the last AF ablation procedure. All patients recovered without major residual impairment.

Discussion

Our study reveals several important findings. First, it confirms that termination of PsAF can be achieved in most patients using a stepwise ablation strategy. Second, by five years of follow-up, freedom from arrhythmia recurrence is modest with a single ablation procedure, but can be achieved in the majority of patients by repeat ablation as needed. Third, a slow but steady decline in freedom from arrhythmia recurrence is noted during long-term follow up, and predictors of arrhythmia recurrence include failure to terminate AF by ablation, a continuous AF duration ≥18 months, a LA diameter ≥50mm, and structural heart disease.

Long-term Outcome of Persistent AF Ablation

The concept of PVI as a treatment option for PAF is well established, with success rates of up to 80% during long-term follow-up.[1,3]However, significantly less evidence exists for catheter ablation in PsAF patients.[1,6]Knowledge of the long-term outcome of PsAF ablation is paramount to define its role in clinical practice.A recent study reported the long-term clinical outcome undergoing catheter ablation of longstanding PsAF using circumferential PVI in all patients, plus additional substrate modification in limited patients.[6] During 56 and 50 months follow-up, single- and multiple ablation procedure success was 20% and 45%, respectively. Circumferential PVI alone established long-term SR maintainance in only 24% of patients.[6] These results raise the question whether circumferential PVI is the adequate ablation strategy for PsAF.

Haissaguerre et al. first described the stepwise ablation approach in PsAF.[8,9] Using this approach, Rostock et al. reported a success rate of 79% after a median of 2.3 procedures with a median of 27 months of follow-up.[13] Our study is the first to report on 5-year outcome in PsAF ablation aiming at AF termination as a procedural endpoint. To our knowledge, our study reports the highest long-term success rate in patients undergoing PsAF ablation. These results suggest that an ablation strategy beyond PVI may be of value in optimizing outcomes for PsAF.

However, the slow but steady decline in arrhythmia-free survival raises the question of whether ablation provides durable suppression of PsAF. Interestingly, arrhythmia recurred in 30 patients who had maintained SR for ≥1 year. It may be speculated that some recurrences of AF escaped earlier detection and that amiodarone may have masked some AF drivers during the index procedure, which later became manifest. These findings underscore the importance of careful long-term follow-up after AF ablation and have important ramifications regarding anticoagulation after PsAF ablation.

Impact of AF Termination

The other main finding of this study is that termination of PsAF by ablation can be achieved in the majority of patients and is the strongest predictor for freedom from arrhythmia recurrence during follow-up. Termination of AF may therefore represent a valid electrophysiological endpoint during PsAF ablation.

Reports dealing with the impact of AF termination on outcome are inconsistent. AF termination appeared to be a strong predictor of success in several studies.[13,16] However, the rate of PsAF termination by ablation varies significantly between different approaches and centres. Although AF termination occurs in 16% of patients undergoing an anatomically guided circumferential PV ablation, [14]termination rates of up to 87%are reported with the use of the stepwise ablation approach,[8,11-13]including ~20% of PsAF patients in whom PsAF is terminated during RA substrate modification.[11,12]

Clinical Implications

In the broad population of patients with PsAF, the optimal selection for and the strategy of catheter ablation has yet to be determined. Our study suggests that freedom from arrhythmia recurrence can be achieved in65% of patients over five years of follow up by ablation, and in 74% when adding AADs. However, more than one ablation procedure is necessary in the majority of patients. In addition to patients' symptoms, other characteristics such as continuous AF duration, presence of structural heart disease, or LA diameter should be used to decide with the patient if ablation is a viable treatment option. Procedural AF termination may predict favourable outcomes in patients undergoing substrate-based ablation. However, AF ablation in our study was associated with a significant procedural complication rate, consistent with the current world-wide experience with this procedure.[1,22]

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Limitations

The current study describes results from a single experienced centre including a limited number of patients. Due to the high AF termination rate reported in our study, which required long and arduous procedures, these results may not be generalizable to all ablation centers treating persistent AF. Furthermore, these results require confirmation in a randomized controlled trial comparing different PsAF ablation approaches.

Despite complying with recommendations regarding ECG monitoring for PsAF ablation[1] with extensive efforts to detect asymptomatic recurrences, the potential for under-recognition of silent AF remains such that recurrence rates may have been underestimated.

Our study population represents a selected subgroup with persistent AF such that results should not be extrapolated to all patients with persistent AF.

Finally, the optimal ablation strategy for persistent AF remains unknown such that less extensive and more focused procedures may potentially achieve similar long-term efficacy in the future.[23,24]

Conclusions

In PsAF patients, a stepwise catheter ablation strategy with AF termination as a procedural endpoint and with repeat interventions as needed provides acceptable freedom from arrhythmia recurrence over a 5-year follow up period. Procedural failure to terminate AF, PsAF duration ≥18 months, LA diameter ≥50mm, and the presence of structural heart disease are predictors of arrhythmia recurrence. While most recurrences are observed during the first year, a slow but steady decline in arrhythmia-free survival is noted thereafter.

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Conflict of Interest Disclosures: None

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Table 1: Baseline Characteristics (n = 150 patients)

Female gender	27 (18%)
Age (years)	57 ± 10
History of AF (months)	60 (36-120)
Continuous AF duration (months)	13 (7-24)
Long-standing persistent AF	97 (64.7%)
Unsuccessful AADs (Class I & III)	2.1±1.0
Amiodarone at time of procedure	32 (21.3%)
LA diameter (mm)	48 ± 7
LV ejection fraction (%)	58 ± 13
Structural heart disease	64 (42.7%)
Valvular heart disease	24 (16%)
Dilated cardiomyopathy	22 (14.7%)
Ischemic heart disease	20 (13.3%)
Severe LV hypertrophy	12 (8%)
Hypertension	64 (42.7%)
Diabetes mellitus	13 (8.7%)
Prior stroke or TIA	9 (6%)
$CHADS_2$ score = 0	59 (39.3%)
$CHADS_2$ score = 1	54 (36%)
$CHADS_2$ score ≥ 2	37 (24.7%)

Values are given as n (%), mean ± SD, or median (25^{th}-75^{th} percentile). AF denotes atrial fibrillation; AADs, antiarrhythmic drugs; LA, left atrium; LV, left ventricle; TIA, transient ischemic attack.

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Table 2: Factors univariately associated with Arrhythmia Recurrence off Antiarrhythmic Drugs following the last Ablation Procedure

Variable	HR	95% CI	P Value
Age, years	1.034	1.004 - 1.065	0.03
Continuous AF duration, months	1.021	1.015 - 1.027	<0.0001
Diabetes mellitus	2.241	1.048 - 4.795	0.04
Structural heart disease	2.202	1.273 - 3.805	<0.01
LA diameter, mm	1.059	1.010 - 1.111	0.02
Failure to terminate AF during first procedure	2.558	1.605-6.098	<0.001

AF denotes atrial fibrillation; CI, confidence interval; HR, hazard ratio; LA, left atrium.

Table 3: Multivariate Predictors of Arrhythmia Recurrence off Antiarrhythmic Drugs following the last Ablation Procedure

Variable	HR	95% CI	P Value
Failure to terminate AF during first procedure	3.831	2.070-7.143	<0.0001
LA diameter ≥50mm	2.083	1.078 - 4.016	0.03
Continuous AF duration ≥18 months	1.984	1.024 - 3.846	0.04
Structural heart disease	1.874	1.037 - 3.388	0.04

The final model consisted of the variables listed above along with age and diabetes mellitus, which were associated with P-values >0.05 and <0.1. AF denotes atrial fibrillation; CI, confidence interval; HR, hazard ratio; LA, left atrium.

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Figure Legends:

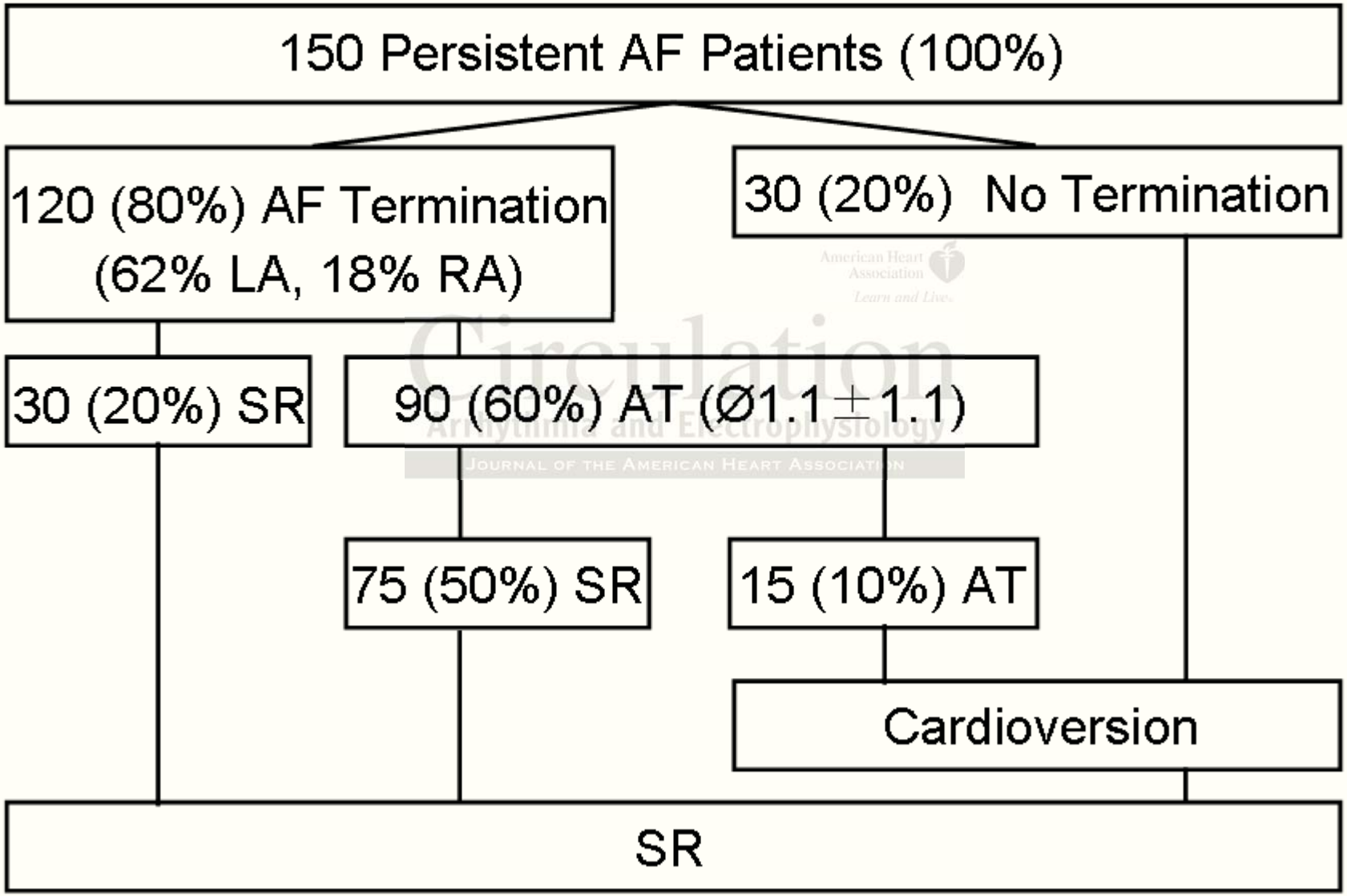
Figure 1: Procedural results of 150 patients undergoing their first AF ablation. AF = atrial fibrillation; AT = atrial tachycardia; DCC = electrical cardioversion; LA = left atrium; RA = right atrium; SR = sinus rhythm.

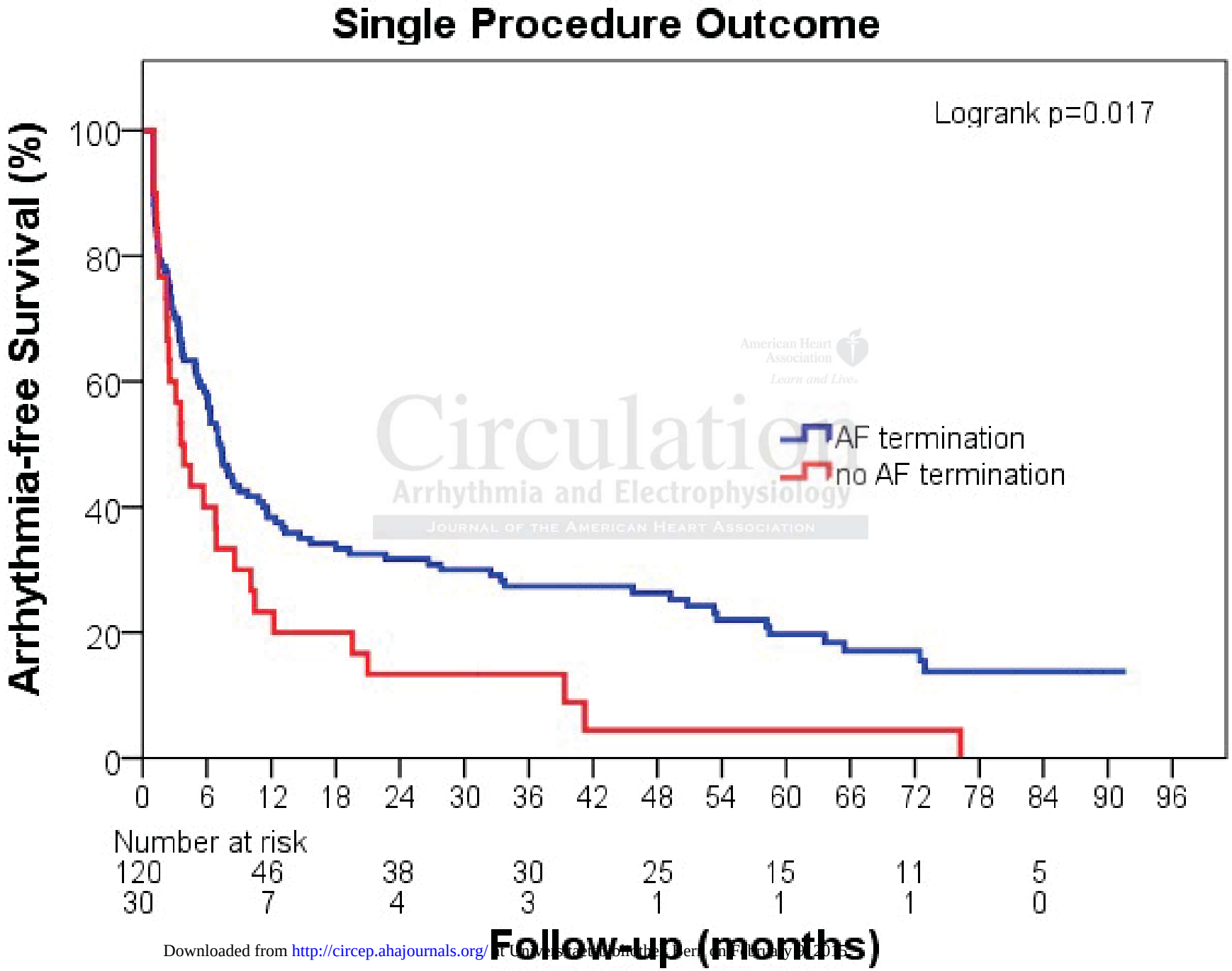
Figure 2: Single procedure success rate off antiarrhythmic drugs. Risk of arrhythmia recurrence was significantly higher in patients who did not terminate AFduring the intervention.

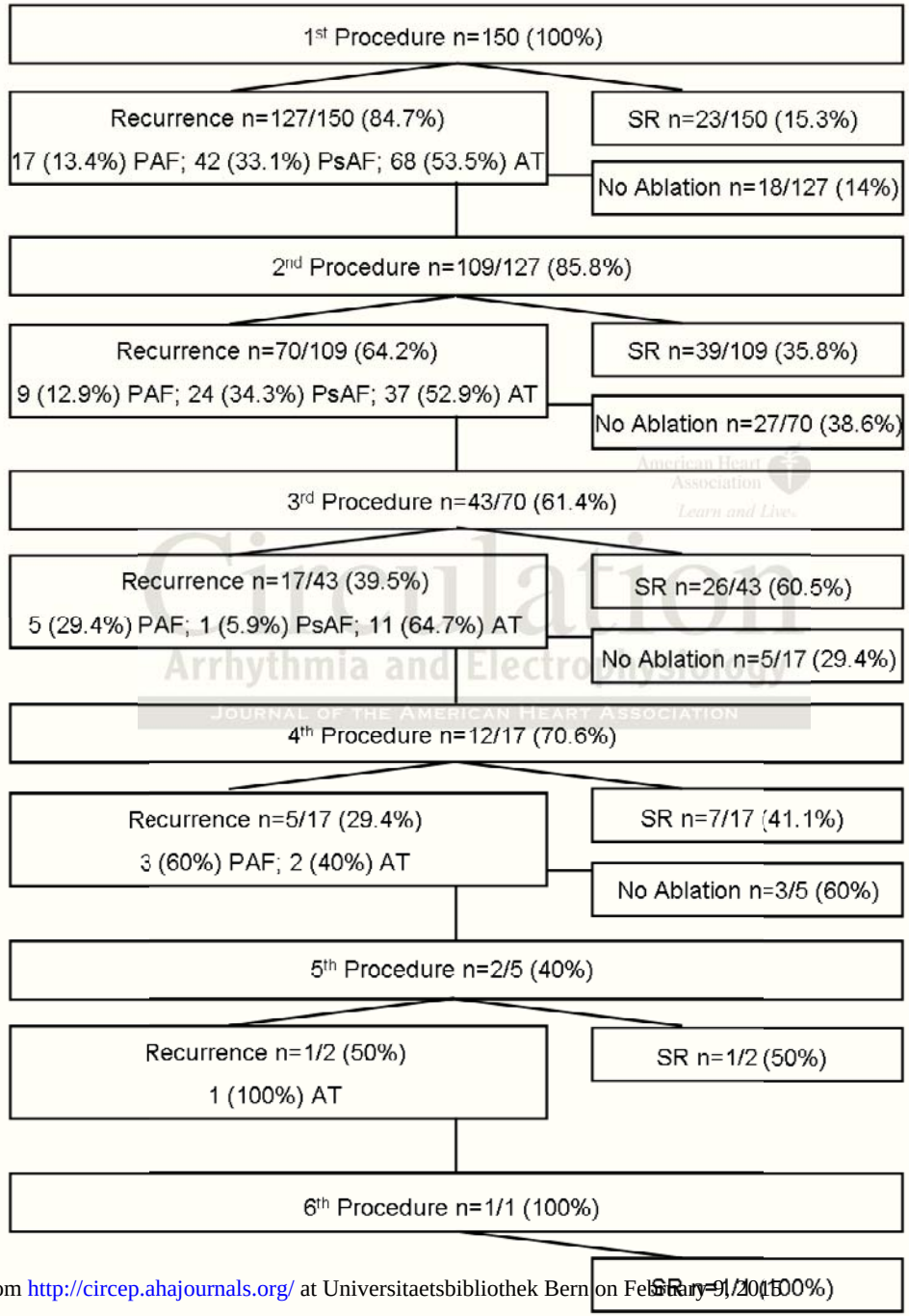
Figure 3: Flowchart demonstrating arrhythmia outcome. AT = atrial tachycardia; PAF = paroxysmal AF; PsAF=persistent AF; SR = sinus rhythm.

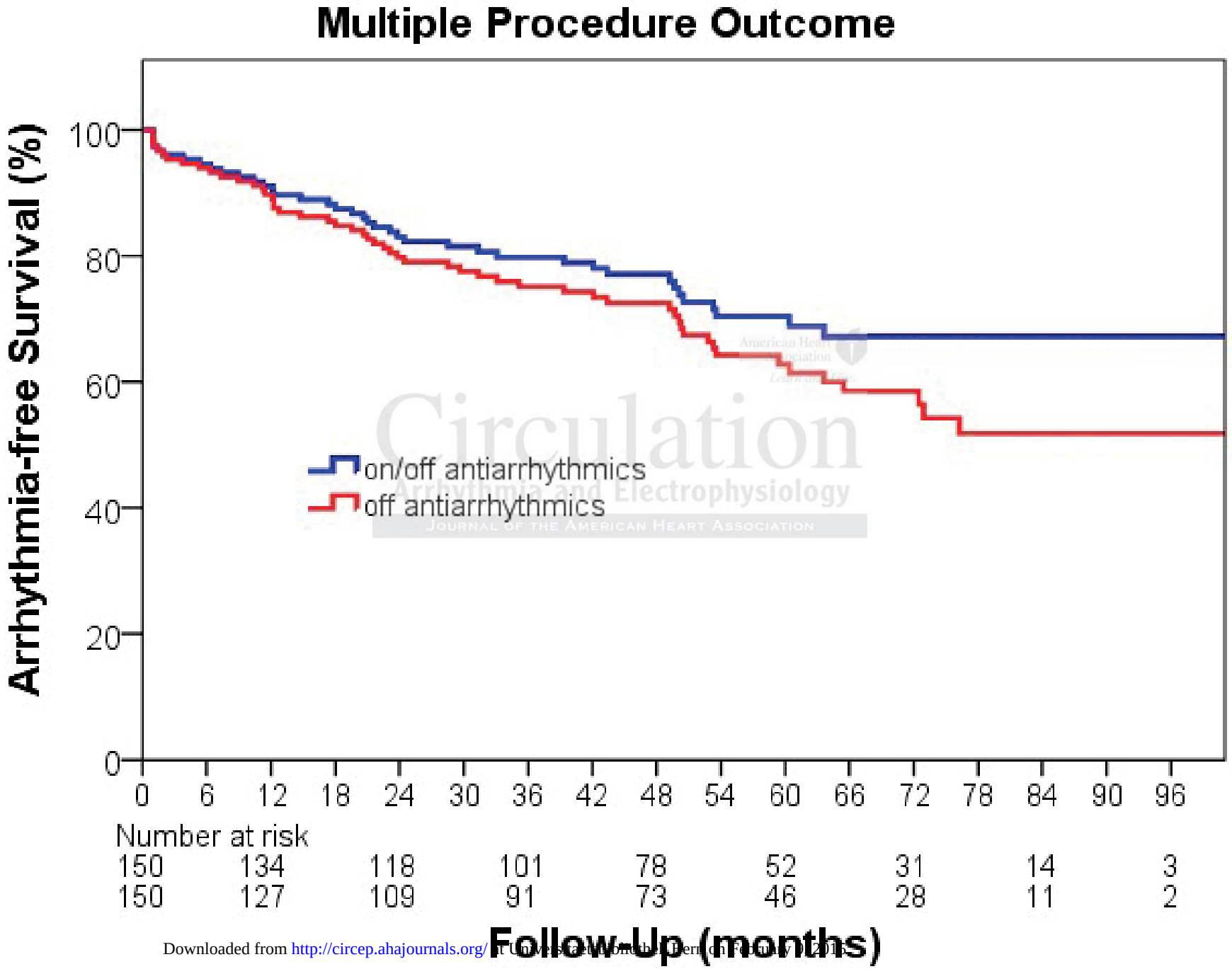
Figure 4: Multiple procedure success rate off and on antiarrhythmic drugs of persistent AF ablation. During a median follow-up of 58 (IQR43-73) months following the last ablation procedure, 97 of 150 (64.7%) patients remained in SR without drugs.111 patients (74%) remained in SR when including patients taking antiarrhythmics.

Figure 5: Multiple procedure success rate off antiarrhythmic drugs according to whether AF was persistent or long-standing persistent (Panel A) and multiple procedure success rate on or off antiarrhythmic drugs according to whether AF terminated directly to sinus rhythm, AF terminated to an atrial tachycardia, or AF did not terminate (Panel B).

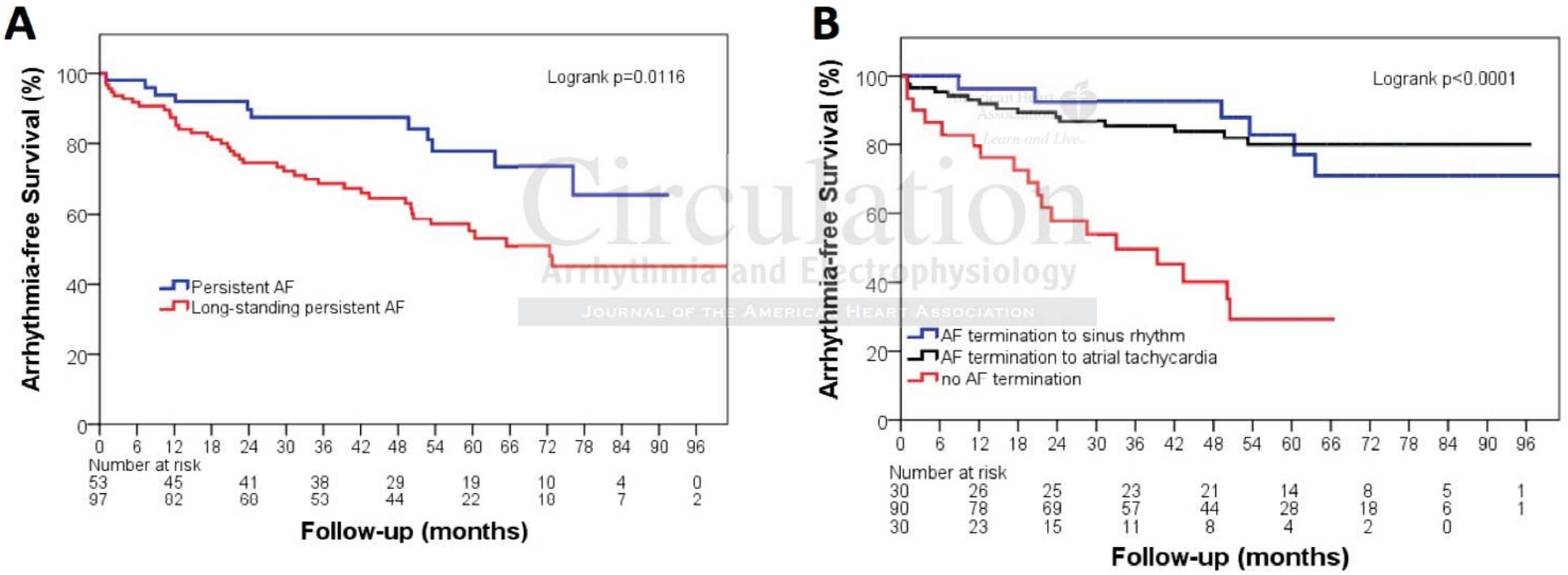








Multiple Procedure Outcome



SUPPLEMENTAL MATERIAL

SUPPLEMENTAL METHODS

Electrophysiological Study and Ablation Procedure

Details of the peri-procedural management and the ablation technique at our institution have been described previously.[1-8] As it is standard clinical practice at our institution, all AADs were discontinued at least five half-lives prior to ablation except for amiodarone (n=32). All patients received oral anticoagulation (target INR 2–3) for ≥1 month prior to the procedure. Patients with a contraindication to warfarin or who refused oral anticoagulation were treated with anti-platelet agents, at their physician's discretion. Patients underwent transesophageal echocardiography within 48h of the procedure to rule out thrombus. Warfarin was restarted the day after the procedure for ≥6 months after each ablation procedure and was continued thereafter at the physician's discretion.

The following catheters were introduced via the right femoral vein: (I) a deflectable quadripolar or decapolar catheter (2–5–2 mm electrode spacing, Xtrem™, ELA Medical™, Le-Plessis- Robinson, France) positioned within the coronary sinus; (II) a 10 pole, fixed-diameter circumferential mapping catheter to guide PVI (Lasso™; Biosense-Webster™, Diamond Bar, USA), introduced with the aid of a long sheath (Preface™, Biosense-Webster™, Diamond Bar, USA, or SLO™, St. Jude Medical™, St. Paul, USA); (III) a 3.5 mm irrigated-tip quadripolar ablation catheter (2–5–2 mm electrode spacing, ThermoCool™, Biosense-Webster™, Diamond Bar, USA). A single trans-septal puncture was performed in AP view with pressure monitoring.

Stepwise ablation was performed in the following sequence: PVI, electrogram-based

ablation, and linear ablation. The desired procedural endpoint was termination of AF without pharmacological or electrical cardioversion.

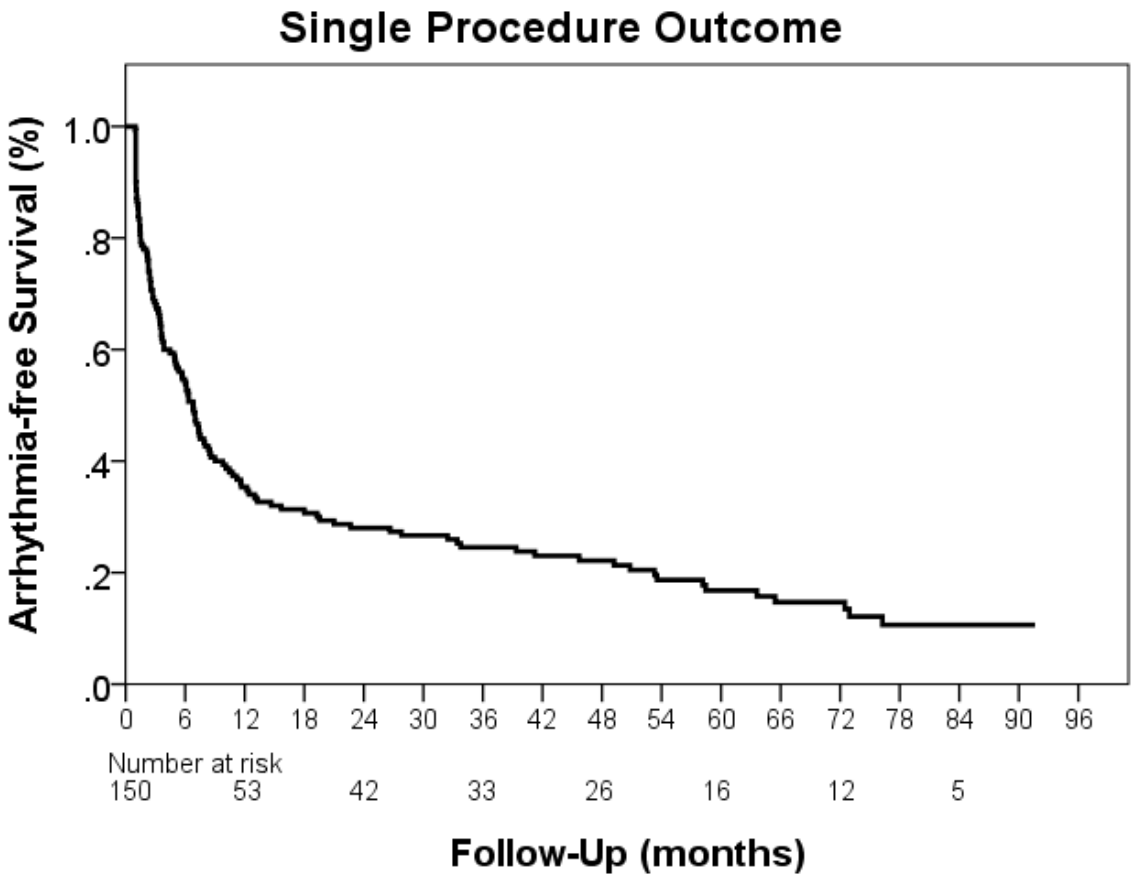
Circumferential PVI was performed with the endpoint of abolition or dissociation of electrical activity of all PVs. When AF did not terminate during PVI, the procedure was continued with electrogram-based ablation in the LA. Ablation targets included all sites in the LA displaying any of the following electrogram features: continuous electric activity, complex rapid and fractionated potentials, sites with an activation gradient between electrograms of the proximal and distal bipoles of the ablation catheter, and sites with local short cycle lengths compared to the LA appendage. The endpoint of ablation in each region was transformation of complex into discrete electrograms and slowing of local cycle length compared with LA appendage or elimination of electrograms. The RF delivery was also stopped after 60 sec of application per site.

When ablation of the inferior LA did not result in organization of the coronary sinus, additional ablation within the coronary sinus was performed, using the same electrogram-based criteria. Linear ablation was performed if AF persisted following the previous ablation steps. A roof line was performed joining the right and left superior PVs, and if AF continued, a mitral isthmus line from the mitral annulus to the left inferior PV was performed, with the endpoint of abolition of local electrograms.

Mapping and ablation using the same electrogram-based criteria were continued in the right atrium (RA) if AF did not terminate during LA ablation and the RA appendage demonstrated a shorter cycle length than the LA appendage. Linear ablation was performed in all patients at the cavotricuspid isthmus either before or after restoration of SR and bidirectional conduction block was confirmed.

SUPPLEMENTAL FIGURE

Supplemental Figure 1: Single procedure success rate off antiarrhythmic drugs.



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Five-Year Outcome of Catheter Ablation of Persistent Atrial Fibrillation Using Termination of Atrial Fibrillation as a Procedural Endpoint

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