Arrhythmia Termination Versus Elimination of Dormant Pulmonary Vein Conduction as a Procedural End Point of Catheter Ablation for Paroxysmal Atrial Fibrillation

A Prospective Randomized Trial

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Background—Pulmonary vein isolation (PVI) is still associated with a substantial number of arrhythmia recurrences in paroxysmal atrial fibrillation (AF). This prospective, randomized study aimed to compare 2 different procedural strategies.

Methods and Results—A total of 152 patients undergoing de novo ablation for paroxysmal AF were randomized to 2 different treatment arms. The procedure in group A consisted of PVI exclusively. In this group, all isolated PVs were challenged with adenosine to reveal and ablate dormant conduction. In group B, PVI was performed with the patient either in spontaneous or in induced AF. If AF did not terminate with PVI, ablation was continued by targeting extra-PV AF sources with the desired procedural end point of termination to sinus rhythm. Primary study end point was freedom from arrhythmia during 1-year follow-up. In group A, adenosine provoked dormant conduction in 31 (41%) patients with a mean of 1.6±0.8 transiently recovered PVs per patient. Termination of AF during PVI was observed in 31 (65%) patients, whereas AF persisted afterward in 17 (35%) patients. AF termination occurred in 13 (76%) patients by AF source ablation. After 1-year follow-up, significantly more group B patients were free of arrhythmia recurrences (87 versus 68%; P=0.006). During redo ablation, the rate of PV recondution did not differ between both groups (group A: 55% versus group B: 61%; P=0.25).

Conclusions—Elimination of extra-PV AF sources after PVI is superior to sole PV isolation with the adjunct of abolishing potential dormant conduction.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT02238392.

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Key Words: arrhythmias, cardiac ■ atrial fibrillation ■ catheter ablation ■ follow-up studies ■ pulmonary veins

Despite intensive research during the past 15 years in the field of catheter ablation for paroxysmal atrial fibrillation (AF), recurrence rates after pulmonary vein isolation (PVI) remain as high as 30% to 40% after a single procedure even in highly experienced centers.1–3 Two different mechanisms have been basically identified to be responsible for this procedural limitation: (1) electric recovery of initially isolated PVs and (2) previously unidentified (or newly generated) arrhythmogenic sources outside the PVs.4 Thus, efforts to overcome these limitations have been focused on techniques to enhance the durability of PV isolation and the identification of arrhythmogenic extra-PV sources, respectively. Even though potential risk factors that place the individual patient on an increased risk to experience electric PV recovery could not be identified to date, the intravenous challenge of adenosine was found to reveal a transient dormant PV conduction. On the contrary, the potential existence of arrhythmogenic substrates remote from the PVs was evaluated by the assessment of AF inducibility, either through atrial burst pacing or administration of isoproterenol.5,6 However, the impact of these different techniques on the clinical outcome after a single procedure is still unclear because different studies on these topics...
ADENOSINE VS AF TERMINATION IN PAF ABLATION

WHAT IS KNOWN

• Adenosine can provoke transient “dormant” pulmonary vein conduction and elimination of “dormant” conduction improves the procedural success
• In a subset of patients, extrapulmonary vein sources are responsible for arrhythmia recurrences

WHAT THE STUDY ADDS

• Pulmonary vein isolation alone does not terminate paroxysmal atrial fibrillation in some patients, indicating the presence of extrapulmonary vein sources
• Termination of atrial fibrillation by ablation of extrapulmonary vein sources is superior as compared to elimination of “dormant” conduction in terms of an arrhythmia-free long-term outcome

revealed heterogeneous and controversial results.7 Therefore, the optimal procedural strategy beyond PVI remains to be determined.

The aim of this prospective, randomized study was to evaluate the efficacy of 2 different procedural strategies, elimination of dormant conduction versus elimination of inducible extra-PVI AF sources, in terms of single-procedure 1-year arrhythmia-free outcome in patients with paroxysmal AF.

Methods

Study Population

This prospective, randomized study comprised a total of 152 patients with symptomatic paroxysmal AF refractory to at least 1 antiarrhythmic drug. The study patients were enrolled between January 2012 and January 2013. The mean age was 64±9 years and 88 (58%) were men. All patients were referred for an interventional treatment of paroxysmal AF. A detailed diagnostic work-up was performed by the institutional review board and the ethics committee of the Landesärztekammer Rheinland-Pfalz (837.456.13 (9141-F)). All antiarrhythmic drugs, with the exception of amiodarone, were ceased at least 5 half-lives before the procedure.

Study Protocol

Paroxysmal AF was defined according to the current guidelines.8 However, patients with AF episodes lasting >48 hours that required electric cardioversion were excluded from the study. All patients were characterized by self-terminating episodes with at least 1 documentation in Holter-ECG. The patients were randomized in a 1:1 fashion into 2 groups before the procedure:

Group A

A standardized PVI was performed. In this group, AF was not induced intentionally. When the patient was in spontaneous AF that did not terminate during PVI, the patient was cardioverted. After demonstration of PVI, all PVs were challenged to adenosine.

Group B

In this group, a standard PVI was performed with the patient either in spontaneous or induced AF. If AF did not terminate by PVI, ablation was continued by targeting specific electrogram patterns and behavior with the desired procedural target of termination to sinus rhythm (SR) (Figure 1A).

Ablation Procedure

The procedures were performed under sedation with propofol infusion. The presence of left atrial thrombi was excluded by transesophageal echocardiography in the electrophysiological laboratory directly before the procedure. All patients underwent a standardized PVI procedure. The following catheters were introduced via a right femoral vein access: (1) A steerable decapolar catheter (Inquiry; BI, Irvine Biomedical, Inc, Irvine, CA) was positioned within the coronary sinus; (2) a circumferential decapolar diagnostic catheter (Lasso; Biosense-Webster, Diamond Bar, CA) for mapping of the pulmonary veins; and (3) a 3.5 mm externally irrigated-tip ablation catheter (Thermocool; Biosense-Webster). Access to left atrium was achieved by a single transseptal puncture with the 2 catheters placed into the left atrium via the same puncture. A single bolus of 50 IU/kg body weight heparin was administered after transseptal puncture. The activated clotting time was assessed every 30 minutes and maintained within a range of 250 to 350 seconds. A temperature probe was positioned in the esophagus, and the endoluminal temperature was monitored throughout the procedure. For anatomic guidance, a 3-dimensional reconstruction of the left atrium and the PVs was created using the NavX system (St. Jude Medical, Inc, St. Paul, MN). A circumferential lesion was created around the ipsilateral lateral PVs to achieve simultaneous isolation. PVI was defined by elimination or dissociation of PV potentials recorded on the circumferential PV catheter.

Ablation was performed with a maximum power output of 30 W using an irrigation rate of 10 to 30 mL/min (0.9% saline infused with the CoolFlow Pump; Biosense-Webster) At the posterior wall, the power was reduced to 25 W. In the coronary sinus, the radiofrequency energy was limited to a maximum of 25 W with a manually adjusted irrigation rate to keep the tip-temperature below 42°C.

Adenosine Testing

After demonstration of PVI, all PVs were tested for the presence of dormant conduction by intravenous administration of ≥10-mg adenosine and incremental values increased by 5-mg steps were used until complete AV block was achieved. The induction of ≥3 blocked P waves or a sinus pause of ≥3 seconds was considered to demonstrate an appropriate adenosine dosage. Dormant PV conduction was defined as the transient reappearance of PV activity as recorded in the circumferential PV catheter for at least 2 consecutive beats. In case of the occurrence of dormant conduction, the sites of earliest PV activity were targeted by additional radiofrequency applications with a duration of 90 seconds per application. Afterward, adenosine was readministered with the previous dose that induced dormant conduction. Adenosine testing was performed until the demonstration of persistent PVI in all veins.

Procedural Termination of AF

In patients of group B, AF was induced by atrial burst pacing before PVI when the patient did not present in spontaneous AF to the procedure. Burst pacing was started from the midcoronary sinus with a cycle length of 300 ms and gradually shortened until local refractoriness was achieved (loss of local 1:1 capture). If sustained AF was not inducible by at least 3 attempts, the same induction maneuver was performed from the left atrial appendage. After induction, duration of 10 minutes was defined as inducible sustained AF before any ablation was performed. If PV did not convert the patient to SR, the ablation was continued with the desired procedural target of procedural AF termination was achieved. In this regard, electrogram-guided ablation was performed by targeting areas of short AF cycle length, complex fractionated atrial electrograms, centrifugal activation, and electrogram activation gradients between the distal and the proximal electrodes. Evaluation of electrogram behavior was performed by visual inspection, and no automated software was used to define these areas. After AF termination, no attempts at AF reinduction were performed in any of the patients. If AF termination could not be achieved by ablation, an electric cardioversion was used to restore SR.
Follow-Up

All patients were seen regularly every 3 months in our outpatient clinic. Before visits, the patients received at least 2 separate 48-hour Holter-ECGs. A detailed history of the patients’ symptoms suggestive for potential arrhythmia recurrences was taken. In case of undocumented symptoms suspicious for arrhythmia recurrences, documentation by additional external ECG event recordings was performed. A documented symptomatic or asymptomatic arrhythmia episode lasting >30 seconds was defined as recurrence.

An initial blanking period of 3 months was accepted. The antiarrhythmic drug treatment was not reinitiated after ablation. If patients experienced an early recurrence within the initial 3 months after the procedure, antiarrhythmic drugs were reinitiated for the remaining time in the blanking period. However, all antiarrhythmic drugs were ceased.
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group A, Adenosine (n=76)</th>
<th>Group B, AF Inducibility (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>63±10</td>
<td>64±9.11</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>45 (59)</td>
<td>33 (43)</td>
</tr>
<tr>
<td>Follow-up, mo</td>
<td>24.6±4.01</td>
<td>29.16±4.87</td>
</tr>
<tr>
<td>Maximal duration of AF, h</td>
<td>16.2±20.34</td>
<td>15±26.82</td>
</tr>
<tr>
<td>BMI</td>
<td>27.08±3.62</td>
<td>27.40±3.44</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>46 (61)</td>
<td>53 (70)</td>
</tr>
<tr>
<td>LA size, cm²</td>
<td>22.17±5.18</td>
<td>23.24±4.81</td>
</tr>
<tr>
<td>EF, %</td>
<td>54.74±1.61</td>
<td>55</td>
</tr>
<tr>
<td>Heart disease, n (%)</td>
<td>6 (8)</td>
<td>11 (15)</td>
</tr>
<tr>
<td>CHA²DS²-VASC score</td>
<td>1.51±1.26</td>
<td>1.91±1.89</td>
</tr>
<tr>
<td>Failed antiarrhythmic drugs, n (%)</td>
<td>30 (40)</td>
<td>43 (57)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; BMI, body mass index; EF, ejection fraction; and LA, left atrial.

after the end of the blanking period. Patients with an arrhythmia recurrence after the blanking period were considered procedural failure.

The primary study end point was freedom from any atrial tachyarrhythmia occurring after the blanking period during a follow-up of 12 months. Secondary end points were procedural complications, PV recovery during redo procedures, and overall arrhythmia-free survival, respectively.

Statistical Analysis

All continuous variables are reported as mean±SD or medians with ranges, whereas categorical variables were summarized as proportions. Categorical variables were compared using the χ² test. Comparison between groups was performed with either Student t test or the χ² test. Statistical significance was established at P value <0.05. We assumed a 12-month arrhythmia-free survival of 75% in the adenosine group and 55% in patients assigned to the AF termination group. To observe this difference with a power (1−β) of 0.8 and an α-level (α) of 0.05, the inclusion of 88 patients in each group was estimated. The study protocol predefined a substantially unexpected finding which is not in accordance with the study hypothesis as a stopping criterion. After the inclusion of 152 patients, we observed a markedly different outcome when compared with what has been expected by the study hypothesis. Therefore, the Institutional Scientific Review Board decided to terminate the study early after a subsequent interim analysis revealed a significantly better outcome of patients randomized to group B. Time-to-arrhythmia recurrence was estimated using the Kaplan–Meier method and compared using the log-rank test. Statistical analysis was performed with a statistical software package (SPSS, version 22; IBM, Armonk, NY).

Results

Randomization into both groups was performed in a 1:1 fashion. Patient characteristics were well balanced (Table 1). After an interim analysis of 152 patients (85% of the calculated study size), patient inclusion was stopped because the clinical outcome in both groups was markedly different from what has been expected initially. Significant differences between both groups were observed in the opposite way, and the study was finished prematurely.

Procedural Results

A total of 11 patients presented with spontaneous AF to the procedure (group A: 5; group B: 6). Electric isolation of the PVs was achieved in all patients. The mean procedure duration was 126±45 minutes with a mean fluoroscopy time of 23±9 minutes. For PV isolation, procedure duration (123±39 versus 121±49 minutes; P=0.41), fluoroscopy time (22±8 versus 23±9.4; P=0.24), and mean duration of radiofrequency applications (39±11 versus 40±14 minutes; P=0.92) were not significantly different between both groups. However, the overall procedure duration (137±54 minutes; P=0.009), fluoroscopy time (26±10 minutes; P=0.001), and radiofrequency duration (48±18 minutes; P=0.01) were significantly longer in group B patients.

Group A Results (Adenosine Testing)

In group A, 5 patients were in AF at the beginning of the procedure. In 4 patients, AF terminated during PVI, whereas 1 patient required electric cardioversion because of ongoing AF after PVI. Adenosine induced dormant conduction in 31 (41%) patients with a mean of 1.6±0.8 transiently recovered PVs per patient (Figure 1; Table 2). The mean value of adenosine that was required to achieve the desired effect of AV block was 12.4±3.8 mg (range, 10–25 mg). Dormant conduction was equally distributed to all PVs. A mean of 1.5±0.9 additional radiofrequency applications per PV was required to eliminate dormant conduction (Table 3). In 2 patients, transient PV dormant conduction (LSPV in both patients) was still induced by adenosine after 6 additional radiofrequency applications. In these 2 patients, no further attempt was made to eliminate dormant conduction.

Group B Results (AF Termination)

A total of 6 (8%) patients were in spontaneous AF at the beginning of the procedure. Of the remaining 70 patients, 48 (63%) patients were inducible for AF. In 31 (45%) patients, termination of AF occurred during PVI, in 18 (58%) during isolation of the left PVs, and in 13 (42%) during PVI of the right veins. In the 17 (35%) patients with sustained AF after PVI, the procedure was continued with an electrogram-guided ablation as per protocol. Electrogram-guided ablation terminated AF in further 13 (27%) patients, resulting in an overall AF termination rate of 44 of 48 (92%). Termination of AF occurred exclusively in the left atrium (11) and the coronary sinus (2) with a mean radiofrequency duration of 45±39 minutes (Table 4). None of the patients underwent ablation in the right atrium. All patients converted directly into SR without the occurrence of an intermediate subsequent atrial tachycardia. In the 4 patients without AF termination, no early recurrence occurred after electric cardioversion.

Primary End Point: 12-Month Follow-Up

All patients completed the per-protocol end point of a 12-month follow-up. The Kaplan–Meier 1-year arrhythmia-free survival
estimation revealed a significantly better outcome in group B than in group A patients (87% versus 68%; \(P=0.006\)). In group A, arrhythmia recurrences were characterized as paroxysmal AF, atrial tachycardia, and persistent AF in 19, 1, and 2 patients, respectively. Recurrences occurred in group B patients as paroxysmal AF in 8 patients and atrial tachycardia in 1 patient. No patient of group B experienced recurrence of persistent AF. Of the 4 patients without AF termination and subsequent cardioversion during the first procedure, 2 were free of arrhythmia recurrences whereas the other 2 experienced episodes of paroxysmal AF during follow-up and underwent repeat ablation.

### Electrophysiological Findings During Redo Procedures

A total of 36 patients underwent repeat ablation (group A, 24 [67%] patients; group B, 12 [33%] patients). Interestingly, no significant difference in terms of numbers of recovered PVs was observed between both groups (group A, 52 [55%] versus group B, 29 [61%]; \(P=0.52\)). Almost half of PVs (42%) with eliminated dormant conduction during index ablation demonstrated electric recovery during the redo procedure. Of the 2 patients with persistent dormant conduction in the left superior PV, electric recovery was observed in 1 patient whereas the other patient did not demonstrate PV reconnection.

In group A, the repeat procedure was started in AF in 19 patients. In 10 patients, AF terminated during reisolation of the PVs, whereas 9 patients had sustained AF after PVI and electrogram-guided ablation was performed. In group B, 8 patients were in AF at the beginning of the repeat procedure. AF terminated with PVI in 4 patients, whereas AF sustained after PVI in the remaining 4 patients in whom the procedure was continued with electrogram-guided ablation.

In 7 patients of the overall study population, a third procedure was performed for AF recurrences. Only 1 patient had electric PV recovery (2 veins), the remaining 6 patients demonstrated persistent PV isolation. All patients underwent electrogram-guided ablation to terminate AF.

### Overall Follow-Up

During a mean overall follow-up of 18.7±4.5 months after a single procedure, significantly more group B patients were free of arrhythmia recurrences than group A patients (86% versus 55%; \(P<0.001\); Figure 2). Of note, only 2 (12%) patients with further ablation for extra-PV sources after PV isolation during the index procedure in group B experienced recurrences.

With a mean number of 1.3±0.7 procedures and an overall follow-up duration of 20.3±4.6 months after the final procedure, 67 (88%) patients of group A and 70 (92%) patients of group B were free of recurrences (Figure 3).

### Complications

Only 1 serious complication was observed in the entire study population. In 1 group B patient, pericardial tamponade occurred during electrogram-guided ablation that was successfully treated by percutaneous pericardiocentesis. The patient recovered uneventfully and was discharged as scheduled 2 days after the procedure. No other serious side effects were observed, including thromboembolic events, atrioesophageal fistula, and groin complications, respectively.

### Discussion

#### Main Findings

The presented study revealed the following key findings: (1) the procedural target of evaluation for and ablation of extra-PV AF substrates is superior to elimination of adenosine-induced dormant conduction in patients with paroxysmal AF. (2) The occurrence and elimination of dormant PV conduction have limited impact on both: AF recurrence and persistent PV isolation. (3) Arrhythmia recurrence after 2 AF ablation procedures is not associated with electric recovery of the PVs.

#### Strategies to Achieve Durable PV Isolation

The PVs are the predominant source of paroxysmal AF, and electric PV isolation is the mainstay of catheter ablation for AF.\(^7,8\) Arrhythmia recurrences after ablation are mainly attributed to electric PV reconnection with a strong correlation between the clinical magnitude of arrhythmia recurrences and the number and atrial-to-vein conduction delay of the PVs.\(^9\) Thus, significant efforts were made to develop techniques and tools that may help to enhance the durability of PVI after a single procedure. In this attempt, several different strategies

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Table 3. Number of PVs With Dormant Conduction and Number of Additional RF Applications Required to Eliminate Dormant Conduction

<table>
<thead>
<tr>
<th>No. of PVs With Dormant Conduction, n (%)</th>
<th>Mean No. of RF Applications to Abolish Dormant Conduction, n</th>
</tr>
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<tbody>
<tr>
<td>LSPV 14 (7)</td>
<td>2.4±1.7</td>
</tr>
<tr>
<td>LIPV 14 (7)</td>
<td>1.1±0.3</td>
</tr>
<tr>
<td>RSPV 14 (7)</td>
<td>1.1±0.4</td>
</tr>
<tr>
<td>RIPV 8 (4)</td>
<td>2.1±0.4</td>
</tr>
</tbody>
</table>

LIPV indicates left inferior pulmonary vein; LSPV, left superior pulmonary vein; PV, pulmonary vein; RF, radiofrequency; RIPV, right inferior pulmonary vein; and RSPV, right superior pulmonary vein.

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Table 4. Procedural Findings in Group B Patients With Persistent AF After PVI Isolation Requiring Electrogram-Guided Ablation to Achieve AF Termination

<table>
<thead>
<tr>
<th>Patients With AF Termination During Electrogram-Guided Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RF duration for PVI, min</td>
</tr>
<tr>
<td>40±14</td>
</tr>
<tr>
<td>Mean RF duration for Defrag, min</td>
</tr>
<tr>
<td>10±7</td>
</tr>
<tr>
<td>AF termination sites in the LA, n</td>
</tr>
<tr>
<td>Anterior, n</td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td>inferior/lateral, n</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>LAA, n</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>Roof, n</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>Posterior, n</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>AF termination in the CS, n</td>
</tr>
<tr>
<td>2</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; CS, coronary sinus; LA, left atrial; LAA, left atrial appendage; PV, pulmonary vein; PVI, pulmonary vein isolation; and RF, radiofrequency.
were investigated, such as elimination of dormant conduction induced by adenosine,\textsuperscript{10} the implementation of a waiting period after PVI,\textsuperscript{11} contact force-guided ablation,\textsuperscript{12} and PVI with the target of unexcitable circumferential lesions around the PVs,\textsuperscript{13,14} respectively.

After the initial description of adenosine-mediated transient resumption of PV conduction after isolation,\textsuperscript{10} several single-center studies have investigated the impact of dormant conduction elimination on the clinical outcome.\textsuperscript{15,16} However, these studies have shown that neither the elimination nor the absence of dormant conduction provides prognostic evidence of persistent durability of PV isolation. Recently, the incidence of dormant conduction after PVI facilitated by nonexcitable circumferential lesions around the PVs,\textsuperscript{13,14} respectively.

Irrespective to these hypothetical considerations, the application of both techniques has been shown to result in increased success rates.\textsuperscript{21–24} Thus, successful elimination of arrhythmogenic sources acting as reinitiators or perpetuators after PVI is beneficial for a favorable outcome in patients with paroxysmal AF. However, there are also data demonstrating no different outcomes in patients with and without arrhythmia crista terminalis, and the coronary sinus with its endocardial interface, respectively.\textsuperscript{18–20} Because spontaneous activation of AF-initiating triggers is infrequently observed during electrophysiological procedures, provocative maneuvers are required in the vast majority of patients presenting in SR to the procedure. Two fundamentally different strategies are used to evaluate the potential existence of non-PV AF sources after PVI: pharmacological provocation with β-adrenergic agents (eg, isoproterenol) to provoke ectopic arrhythmogenic atrial activity, on the one hand, and AF induction by electric atrial burst stimulation, on the other.

Theoretically, both approaches to reveal extra-PV sources may have mechanistic disadvantages. Pharmacological provocation with β-adrenergic agents will not only provoke a pathological substrate relevant to AF initiation and perpetuation, but also indubitably influence healthy atrial tissue with the potential to transform physiological cell activity into an arrhythmogenic electric behavior with increased automaticity or enhanced susceptibility to AF persistence. Particularly, the latter one will prevent further evaluation of AF-initiating triggers. In contrast, the evaluation of AF inducibility by atrial burst pacing aims to test a potential capability of the atrial substrate to maintain AF with isolated PVs. Moreover, this approach is also based on the concept that the presence of AF will activate extra-PV sources that become apparent with spontaneous ectopic activity or reinitiations after AF termination. Artificial induction of AF, however, also has inherent limitations by the potential to provoke a clinically nonrelevant arrhythmia activity, particularly with repeated AF induction attempts (with AF begets AF).

Evaluation of Non-PV Triggers

The incidence of paroxysmal AF triggered and maintained by non-PV sources has been observed in 20% of patients during index ablation and up to 30% of patients at repeat procedures.\textsuperscript{18} These sources can be located throughout both atria and the great thoracic veins. However, the predominant anatomic sites are the superior vena cava, left atrial free wall, the

**Figure 2.** Kaplan–Meier arrhythmia-free survival estimation during an overall mean follow-up of 18.7±4.5 mo after a single procedure. The vertical line indicates a follow-up duration of 1 y. Group B patients had a significantly better outcome than group A patients ($P=0.006$ based on 12 mo of follow-up; $P=0.001$ based on overall follow-up).

**Figure 3.** Kaplan–Meier arrhythmia-free survival estimation after final procedure (mean of 1.3±0.7 procedures with an overall follow-up duration of 20.3±4.6 mo).
inducibility testing after PVI. Potential reasons for this divergent observation are as follows: (1) AF inducibility after PVI rather identify patients with an enhanced substrate susceptibility because of a progressed electric disease and, therefore, patients at a higher risk for AF progression. (2) Identification and ablation of non-PV triggers are challenging, particularly with the presence of multiple foci, and thus inconsistent data may result from different success rates in the elimination of these triggers.

**Elimination of Dormant Conduction Versus AF Inducibility Testing**

This study revealed a superior benefit of AF inducibility testing versus evaluation and elimination of adenosine-induced dormant conduction. Although we initially hypothesized the opposite, the following reasons may explain the study findings: (1) in the present study, the elimination of dormant conduction did not result in long-term freedom from electric PV recovery. Thus, the number of recovered PVPs identified during the redo procedure did not differ significantly between the adenose and the inducibility group. Therefore, a theoretically beneficial effect of a higher number of persistent isolated PVPs in the adenose group was not achieved. (2) In the inducibility group, AF persisted after PVI in one third of cases. In these patients, extra-PV sources were mapped and ablated with AF termination in more than three fourths. The extended ablation with the elimination of extra-PV sources and a potential debulking of the substrate may have translated into a higher clinical success rate, particularly during the first year after ablation.

Additional studies with ablation strategies that provide a high single-procedure PVI persistence rate will more accurately reveal the true incidence of non-PV sources because the number of patients with persistent isolation of all PVPs during the first redo procedure will certainly increase.

**Limitations**

The presented study has some limitations that may have affected the study findings. First, in the presented study, we used a conventional irrigated-tip catheter without contact-force measurement. However, the use of contact-force catheter may have led to a lower number of adenosine-induced dormant PV reconnection, and thereby to a potentially lower number of PV conduction recurrences during follow-up. Second, in patients who were not inducible for AF before ablation, we did not use isoprenaline or other adrenergic drugs to facilitate AF induction. Thus, extra-PV triggers of AF may have been missed in noninducible patients.

Because the trial was terminated early for efficacy in the absence of prespecified statistical stopping criteria, the nominal P values presented should be interpreted with caution.

**Conclusions**

Evaluation of AF inducibility and elimination of extra-PV AF sources is superior to sole PV isolation with the adjunct of abolishing potential dormant conduction. The elimination of adenosine-provoked dormant conduction is not associated with a durable electric PV isolation in a substantial number of cases.

**Disclosures**

None.

**References**


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