Atrial Fibrillation Cycle Length is a Sole Independent Predictor of a Substrate for Consecutive Arrhythmias in Patients with Persistent Atrial Fibrillation

Running title: Drewitz et al. Substrates for consecutive arrhythmias

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Abstract

Background - Termination of persistent atrial fibrillation (AF) can be achieved through ablation, with the majority of patients terminating to an atrial tachycardia (AT) and fewer directly to SR. We aimed to identify potential predictors for the existence of a substrate for AT upon termination to sinus rhythm (SR).

Methods and Results - We assessed 95 persistent AF patients (60±10 years) who underwent catheter ablation to the endpoint of AF termination. Forty patients terminated directly to SR (SRterm) and 55 to ATs (ATterm). Compared to the ATterm group, the SRterm group were younger (56±10 vs. 63±9 y, p=0.001), had shorter durations of AF before ablation (9±26 vs. 14±20 months, p<0.001), smaller left atrium (LA) diameters (41±5 vs. 45±5 mm, p=0.015) and longer baseline AF cycle lengths (AFCL, 178±23 vs. 159±31 ms, p=0.005). However, AFCL was the sole independent predictor of direct termination to SR. The most frequent AF termination site in SRterm patients were the pulmonary veins (PV, 53%), whereas in ATterm patients this was within the LA (58%). After follow-up of 12±6 months, there was a trend towards a greater proportion of patients in SR amongst those who terminated directly to SR after a single procedure. The most frequent type of recurrence was paroxysmal AF in SRterm patients, and AT in ATterm patients.

Conclusions - Patients who terminate to SR through ablation without an intermediate AT are characterized by a less altered arrhythmogenic substrate. Baseline AFCL emerged as a sole independent predictor of a substrate for consecutive arrhythmias.

Key words: atrial fibrillation, catheter ablation, termination, arrhythmia mechanisms
Introduction

Persistent atrial fibrillation (AF) can be terminated by catheter ablation using a stepwise approach [1-3]. The concept of this procedure is to combine pulmonary vein isolation (PVI), bi-atrial ablation of complex fractionated atrial electrograms (CFAE), and linear lesions [1-3], thus modifying the atrial substrate to one unable to support the fibrillatory process and culminating in arrhythmia organization. The vast majority of patients convert to a regular arrhythmia, reflecting a step forward towards sinus rhythm (SR) [4,5]. However, in a considerable number of patients, AF may terminate directly to SR. The reasons for these different responses to ablation and the potentially divergent epidemiological and electrophysiological characteristics of these two patient cohorts are largely unknown.

The aim of the present study was to characterize potential differences between patients with AF termination to atrial tachycardia (AT) and those who terminate directly to SR during de-novo catheter ablation for persistent AF. Furthermore, we aimed to identify potential predictors for the existence of an arrhythmogenic substrate for consecutive atrial arrhythmias occurring after termination of AF upon conversion to SR.

Methods

Study Population

Between January 2007 and April 2008, a total of 260 consecutive patients were referred for persistent AF ablation. Amongst them, 165 patients were excluded because of previous catheter ablation for AF, failure of AF termination or prior concomitant AF ablation during cardiac surgery. Termination of AF was the targeted procedural endpoint in all ablations. Thus, 95 patients (73 male) undergoing de-novo ablation for persistent AF, whose AF terminated through ablation were included. Forty patients terminated directly to SR during ablation while 55 patients converted into AT upon AF termination. All patients had to be in AF at the beginning of the procedure with a minimum AF duration (defined as the continuous
AF-episode prior to ablation) of one week. All patients had a history of at least one electrical cardioversion.

Epidemiological baseline characteristics including AF-history (defined as the time to the first diagnosis of AF), existence of structural heart disease and echocardiographic parameters were obtained prior to ablation. Furthermore, electrophysiological characteristics and behavior in response to ablation were assessed before and during the procedure. The study was approved by the institutional ethical committee and all patients gave written informed consent. Antiarrhythmic drugs, with the exception of amiodarone, were discontinued at least five half-lives prior to the procedure. Amiodarone was stopped on the day of the procedure.

**Electrophysiological Study**

All patients underwent transesophageal echocardiography to exclude atrial thrombi within 48 hours before the procedure. The procedure was performed under sedation with propofol and fentanyl and under continuous monitoring of blood pressure and peripheral oxygen saturation.

Surface electrocardiogram and bipolar endocardial electrograms were continuously monitored and stored on a computer-based digital amplifier/recorder system (Bard Electrophysiology).

The following catheters were introduced via a femoral vein access: (1) a steerable decapolar catheter (Inquiry, IBI, Irvine Biomedical Inc.) was positioned within the coronary sinus (CS); (2) a decapolar diagnostic catheter for circumferential mapping of the PVs (Lasso, Biosense-Webster); (3) a non-steerable quadripolar diagnostic catheter (Inquiry, IBI, Irvine Biomedical Inc.) was positioned in the right atrial appendage (RAA); and (4) a 3.5 mm externally irrigated-tip ablation catheter (ThermoCool, Biosense-Webster) was used for mapping and ablation. The Lasso and ablation catheters were stabilized by long sheaths (SL0, Daig Inc., St. Jude Medical) continuously flushed with heparinized saline solution. Access to
the left atrium (LA) was achieved by a single transseptal puncture with the two catheters placed into the LA via the same transseptal puncture. A single bolus of 50 IU/kg body weight heparin was administered after transseptal puncture and during the procedure the ACT was maintained > 250 seconds.

**Radiofrequency Ablation**

The ablation procedure was performed using a sequential ablation approach as has been previously described in detail [3]. RF current for PV isolation (PVI) was applied with a maximum power output of 30 W, with 35 W in the LA, and up to 30 W in the RA. Ablation within the CS was performed with a maximum of 25 W. The maximum RF duration for one application was 180 seconds. The ablation catheter irrigation rate was manually adjusted to keep the temperature below 42°C.

**PV Isolation**

Circumferential PVI was always performed as the first step with a technique that has also been previously described in detail [6]. Isolation of the PVs was performed with the guidance of a circumferential mapping catheter. Circumferential ablation was applied within the antrum of the LA, 1 to 1.5 cm proximal to the PV ostia with the aim of simultaneous isolation of the ipsilateral pair of PVs. Additional applications were applied within the circumferential lesion set to complete isolation, e.g. at the PV carina, if pair isolation had failed. All PVs were mapped again with the circular mapping catheter at the end of the procedure in SR and re-isolated in case of early recovery.

**LA Defragmentation**

When AF did not terminate during PVI, the procedure was continued with LA defragmentation as has been described previously [1,3,6,7]. Ablation targets included all sites displaying any of the following electrogram features: continuous electrical activity [8],
complex fractionated potentials [9], sites with an activation gradient between electrograms of the proximal and distal bipoles of the ablation catheter [10,11], regions with considerably short cycle lengths (CL) and centrifugal activation spreading from a distinct site. The endpoint of ablation was termination of AF to either SR or an organized AT with a stable CL and a consistent atrial activation sequence. Virtually all parts of the LA were explored and considered to potentially harbor areas critical for AF perpetuation and were targeted for ablation if appropriate.

**CS Ablation**

If AF persisted after LA defragmentation with an increase of the local AF cycle length (AFCL), the ablation was continued in the CS. Ablation would commence in the distal CS while the catheter was continuously withdrawn towards the CS ostium during ablation. The endpoints were local organization of electrical activity, slowing the AFCL, electrical disconnection of the CS (represented by local dissociation) or AF termination.

**RA Ablation**

The final step for all patients without AF termination during PVI, LA and CS ablation was right atrial ablation. The targets and endpoints were similar to those for the LA. The SVC was mapped with the roving mapping catheter in all cases in order to identify potential AF drivers. Electrical isolation was attempted if the AFCL in the SVC was shorter than AFCL in the RA.

**Linear Lesions**

In patients who terminated into consecutive ATs, these were mapped and targeted for ablation. In case of macro-reentrant mechanisms (e.g. perimitral flutter, LA roof dependent flutter), linear lesions were applied with the aim of achieving bidirectional block. These lesions were not created in patients who showed only focal or “localized reentrant
tachycardias”. If AF terminated directly to SR during the procedure, no additional linear lesions were delivered.

*Ablation Effects and Measurement of AF Cycle length*

The effect of ablation was monitored by evaluation of the AFCL within the CS and both atrial appendages. The AFCL was measured manually with online calipers by averaging 10 consecutive beats at three different times during an observation period of 1 minute. The mean AFCL was defined as an average of the AFCL measured in the CS and both atrial appendages. The AFCL was obtained prior to and after each ablation step and just before AF termination. Termination of AF was defined as a direct termination to SR or conversion to an organized AT. After achievement of SR, no stimulation maneuvers were performed to test re-inducibility.

*Mapping of Atrial Tachycardias*

AF was defined as beat-to-beat variability in CL and an alternating endocardial activation sequence. Atrial tachycardia was defined as an organized atrial rhythm with a stable CL, a consistent atrial activation sequence in both atria and a monomorphic P wave. When AF converted to a regular arrhythmia, activation and entrainment mapping was performed to differentiate between focal and reentrant mechanisms. A macroreentrant mechanism was defined by demonstrating the entire CL within the respective chamber, entrainment mapping with concealed fusion and a post pacing interval (PPI) ≤ 20 ms longer than the ATCL. Focal AT was defined as consistently early endocardial activity at a site with centrifugal activation. “Localized reentry” was defined as an AT by a consistent PPI and a local electrogram spanning ≥ 80 % of the AT cycle length [4,12] which was eliminated by a discrete ablation. Whenever AF terminated to subsequent ATs, these were targeted for
ablation until SR was achieved. When SR had not been restored by ablation, the AT was terminated by external cardioversion.

**Follow-Up**

Antiarrhythmic drug treatment was discontinued after the index procedure in all patients. A blanking period was not used in this study, every AF or AT episode was documented and considered as recurrence during follow-up.

Patients were seen every 3 months for clinical review and ambulatory Holter monitoring. In between these intervals, the patients were monitored by their referring physicians who performed additional 12-lead ECGs. A successful outcome was defined as the absence of asymptomatic arrhythmia documentation (AF or AT) with a minimal duration of 30 seconds in the Holter ECG and freedom of symptomatic arrhythmia recurrences. In case of non-documented symptoms suspicious for recurrences, documentation by additional Tele ECG recording was achieved.

If patients remained in SR for 12 months without any antiarrhythmic drugs, cessation of anticoagulation was considered.

**Statistical Analysis**

All continuous variables are reported as mean ± SD and/or medians with ranges, while categorical variables were summarized as proportions. Categorical variables were compared using the chi square test. Comparison between groups were performed with either Student’s \( t \)-test or the chi square test. For the logistic regression analysis, the continuous variables were appropriately transformed when required to render them normally distributed. The 95% confidence limits of correlation coefficients were determined by Fisher’s \( r \)-to-\( z \) transformation. Statistical significance was established at p-value < 0.05.
Results

Procedural Data

The procedure-related data are presented in Table 1. To achieve SR, mean procedure and fluoroscopy times were significantly shorter in patients who terminated directly to SR (SRterm) compared to patients who converted via AT (ATterm). The mean duration of RF application needed for AF termination did not differ significantly between both groups (4247 ± 1281 sec vs. 4447 ± 1183 sec, p = 0.237).

Epidemiological Data

Epidemiological and electrophysiological data of the two comparison groups are presented in Table 2. Patients who terminated directly to SR had significantly shorter durations of AF episodes prior to ablation, longer baseline AFCL, fewer prior cardioversions, were younger and had significantly smaller LA diameters. Patients with long standing persistent AF (continuous AF duration > 12 months) were more common in the ATterm group (N = 17, 31%) compared to the SRterm group (N = 5, 12.5%, p = 0.037). There were no significant differences in left ventricular ejection fraction and AF history between the two groups.

Co-morbidities, such as hypertensive heart disease (80% in each group) and coronary disease (16% in SRterm and 10% in ATterm) were equally prevalent in both groups. Both groups had a similar number of patients on antiarrhythmic treatment with amiodarone prior to the procedure (35% of the SRterm patients vs. 36% in the ATterm group).

AF Termination during Ablation

Among the 40 patients with direct termination to SR, AF termination occurred in 21 (53%) patients during pulmonary vein isolation (1\textsuperscript{st} PV: 9%, 2\textsuperscript{nd} PV: 38%, 3\textsuperscript{rd} PV: 29%, 4\textsuperscript{th}...
PV: 24%). Ablation for defragmentation of the LA resulted in direct termination to SR in 13 (33 %) patients (during ablation of the LA roof in 4 patients, anterior wall in 3 patients, the septum in 2 patients and the lateral wall, inferior LA, posterior wall and base of the LAA in 1 patient each). Defragmentation of the CS led to termination directly to SR in 2 patients (5 %) and during RA ablation in 4 patients (10 %, 2 at the RA septum, 2 at the anterior RA). The sites of termination directly into SR are illustrated in Figure 1 with an example of typical intracardiac tracings presented in Figure 2 A-C.

In the 55 patients with AF conversion to AT, the ablation site resulting in AF termination to AT was the LA in 32 patients (58%), the RA in 16 patients (29%), the CS in 5 (9%) and the PVs in 2 (4%). A detailed description of the termination sites is given in Table 3 and Figure 1.

None of the patients in this study required electrical isolation of the superior caval vein.

**Mapping and Ablation of Atrial Tachycardias**

In the 55 patients with AF termination to AT, a total number of 87 consecutive arrhythmias occurred, with a mean number of 1.7 ± 0.8 (range 1 – 4) ATs per patient. These ATs were characterized as focal in 33 (38 %) and reentrant in 54 (62 %) cases. Focal ATs were localized to the LA in 21 (64 %) patients, the RA in 8 (24 %) and the CS in 4 (12 %). Macreentrant ATs consisted of LA roof-dependent flutter (n = 18, 33 %), perimitral flutter (n = 10, 19 %), and cavotricuspid isthmus flutter (n = 14, 26 %). Furthermore, reentrant ATs could be demonstrated to have an anterior or septal circuit in 5 (9 %) and 3 (6 %) patients, respectively. Localized reentrant ATs confined to the ridge of the LAA were seen in 4 (7 %) patients.

Termination of AT to SR by ablation was attempted in all cases. Restoration of SR by elimination of all subsequent ATs was achieved through ablation in 32 of the 55 patients
(58%). In these patients, at least one AT was targeted for ablation (Figure 3 A-C). In 20 patients (36%), SR was restored by external cardioversion due to exceedingly long procedure duration or a markedly high volume of fluid administration through the externally irrigated-tip ablation catheter. Furthermore, the likelihood of successful termination of the current AT was crucial in deciding whether to cardiovert or to continue mapping and ablation. In 3 patients, SR occurred during entrainment mapping and AT was not re-induced.

**Impact of Ablation on Atrial Fibrillation Cycle Length**

Termination of AF was preceded by an increase of the mean AFCL in all patients. In SRterm patients, ablation resulted in prolongation of an initial mean AFCL of 178 ± 23 ms to a mean AFCL of 258 ± 61 ms immediately prior to AF termination. Conversion from AF to AT was accompanied by an increase of the mean AFCL from 159 ± 31 ms to 237 ± 41 ms.

**Predictors of Termination directly to SR**

On univariate analysis, baseline AFCL, LA size and number of cardioversions were significant predictors of termination directly to SR (Table 4). However, in a multivariate regression model that includes all predictors, baseline AFCL was the sole significant predictor of termination directly to SR, with an adjusted odds ratio of 1.110 (95% CI 1.032 - 1.193).

**Adverse Events**

One patient developed pericardial tamponade after PVI which was successfully managed by percutaneous pericardiocentesis. There were no other complications.

**Follow-Up**
During a mean follow-up of 12 ± 6 months (Median 11, range 3-27) after the index procedure, there were more patients who were free of arrhythmia recurrences after a single procedure in the group that terminated directly to SR than those who converted to AT, although this trend did not reach statistical significance (57% vs. 38 %, p = 0.097).

The mode of arrhythmia recurrences was markedly different between the two groups. While ATterm patients mainly experienced ATs as the recurrent arrhythmia, the majority of SRterm patients with recurrences characteristically demonstrated transformation from persistent to paroxysmal AF, all of which episodes lasted less than 24 hours and did not require cardioversion. Only 2 (5%) patients of the SRterm group presented with their original arrhythmia (persistent AF) during follow-up. Follow-up details are presented in figure 4. The comparison of outcome between patients with long standing persistent AF versus those with AF durations of less than 12 months within the two groups did not reveal statistically significant differences.

Overall, there were significantly more ATterm patients on class 1 or 3 antiarrhythmic drug therapy at the time of follow-up than SRterm patients [24 (44%) vs. 4 (10%); p < 0.001]. This therapy was reinitiated due to documented or symptomatic recurrences of AF or AT. Only 4 SRterm patients were on class 1 or 3 antiarrhythmic therapy. Of these, 3 patients had recurrences of paroxysmal AF and one was arrhythmia-free on treatment. The 24 ATterm patients treated with class 1 or 3 antiarrhythmics presented with recurrent ATs in 11 and AF in 6 cases (4 PAF, 2 pers. AF), whereas 7 patients were in stable SR on treatment.

**Electrophysiological Findings at the First Redo Procedure**

Most of the patients with AF or AT recurrences consented to a redo-procedure (1 patient in each group declined). The mean time interval between index and redo procedure was 6 ± 3 months. Electrical recovery of at least 1 PV was observed in all patients (SRterm: 3.0 ± 1.0 PVs, ATterm: 1.5 ± 0.9; p < 0.001). There were significantly more patients in the
SRterm group who required only PV re-isolation to become non-inducible during the redo procedure as compared to the ATterm group [9 (53%) vs. 1 (3%); p < 0.001]. Furthermore, 17 (50%) patients of the ATterm group required ablation of AT after PV re-isolation while none of SRterm patients had a recurrent AT requiring ablation at the redo procedure.

**Discussion**

This study demonstrates some fundamental characteristics of patients with persistent AF and without a preexisting substrate for AT whose AF terminated during stepwise ablation. Patients categorized as persistent AF who terminated directly to SR showed characteristics more typical of patients with paroxysmal AF – they were younger, had shorter AF duration, longer baseline AFCLs and smaller LA dimensions and often required no more than PVI to achieve SR during ablation. However, about half of these patients needed additional atrial defragmentation after PVI to achieve direct termination to SR. Thus, a remarkable number of patients with direct AF termination to SR harbor arrhythmogenic sources beyond the PVs capable for AF perpetuation but do not have a substrate to support subsequent ATs. The observation that a similar quantity of ablation was required to achieve AF termination in both groups may imply that preexisting factors exist in some patients which predispose them to AT upon AF termination. Finally, this study revealed that AFCL was the only independent predictor of termination to SR and thus the absence of a substrate for consecutive arrhythmias.

**Mode of Atrial Fibrillation Termination**

Termination of persistent AF by ablation has emerged as a critical procedural endpoint [2,3,13]. It has the advantage of being predictive for a favorable long-term outcome after ablation and thus provides a procedural goal with prognostic value. However, the rate of AF termination by ablation varies significantly with different approaches and most likely depends
on the extensiveness of ablation and what is perceived as a “satisfactory” procedural endpoint. While AF termination occasionally occurs in 16% of patients undergoing an anatomically guided circumferential PV ablation [14], termination rates between 77 and 87% are reported with the use of the stepwise ablation approach [1-3]. Oral et al [15] reported on 100 patients with persistent AF treated by CFAE ablation with AF termination in 16 patients, of whom 12 (75%) converted directly into SR. In another study by the same group, an AF termination rate of almost 25% was achieved when AF termination was specifically targeted as a desired procedural endpoint with a relatively high number of patients (40%) terminating directly to SR [16]. In contrast, when higher AF termination rates were achieved using the more extensive stepwise ablation approach, the proportion of patients terminating directly to SR without the occurrence of an intermediate AT ranged between 12 and 17% [1-3, 10].

The results of the present study revealed that patients with direct termination to SR demonstrate epidemiological and electrophysiological characteristics similar to patients with paroxysmal AF. Thus, these patients with a clinical presentation of persistent AF and a less altered arrhythmogenic substrate may represent a distinct subgroup of this arrhythmia entity. Although previous studies did not provide specific data on the group of patients with direct termination to SR, it is likely that a considerable number of those patients were characterized by the typical features of this subgroup as described in the current study. It is plausible that these patients constituted the majority of patients with AF termination in studies with a moderate termination rate [15,16]. This, in turn, would also explain the relatively high number of patients with direct conversion to SR observed in these studies.

The Substrate of Persistent AF and Subsequent Atrial Tachycardias

One of the key findings of this study is that baseline AFCL was a sole independent predictor of the mode of AF termination. Thus, a short baseline AFCL predicted the occurrence of a subsequent arrhythmia upon termination to SR and, thereby, the existence of a substrate for consecutive AT. It is perhaps surprising that increasing LA dimension, a
recognized marker of LA disease and chronicity of AF, was inferior to AFCL as a predictor for the occurrence of consecutive AT. This finding has three clinical implications: first, a longer AFCL is known as an independent predictor of AF termination directly to SR, which has a trend towards a better clinical outcome [17]. Second, a shorter AFCL may be a marker for the existence of an arrhythmogenic substrate for AT. Third, the electrophysiological properties of the atria, as reflected in the AFCL, are more relevant marker of AT substrates than the purely anatomical properties reflected in LA dimensions.

Atrial fibrillation is associated with specific alterations of the cellular electrophysiological properties and the macroscopic architecture of the atria, both of which deteriorate with time resulting in a self-sustaining arrhythmia [18]. Accordingly, patients with persistent AF have larger LA diameter, lower mean atrial voltage, pronounced heterogeneity of refractoriness and shorter AFCLs [18-20]. These changes based on an arrhythmia-related remodeling process are considered to represent the substrate of persistent AF. From an electrophysiological aspect, the AFCL is one of the most interesting markers for arrhythmia complexity and advanced electrical alterations of AF. Patients with persistent AF have significantly shorter baseline AFCL than those with paroxysmal AF, and AFCL has also emerged as a predictor for AF termination of persistent AF by ablation [10,17,21].

In a study using computer simulation of AF, an inverse relation between the number of arrhythmogenic sources operating in persistent AF and the AFCL could be demonstrated, i.e. a higher number of sources was associated with shorter AFCL [21]. Not surprisingly, AFCL can also be used as a surrogate parameter for the effect of ablation on the arrhythmic process as an indirect marker for the extinction of sources [21,22]. Thus, AFCL does not only reflect local refractoriness, but perhaps more importantly the activity and burden of arrhythmogenic sources operating in persistent AF [22].

The observation that epidemiological and electrophysiological properties of ATterm patients are more typical of those with persistent AF suggests that the arrhythmia substrates in these two distinct atrial arrhythmias (AF and AT) have common entities. Thus, it is plausible
that advanced structural and electrical alterations in these patients reflect a more complex arrhythmogenic process which requires the elimination of more sources [22,23]. The ablation of these sources resulting in AF termination may simply eliminate the “final common pathway” of the fibrillatory process by “unmasking” the underlying AT. This theory is in keeping with a tentative hypothesis gained from the computer simulation studies that AFCL may be the result of the summation of activities/sources acting simultaneously during AF at any given time in the site measured [21].

The findings of this study may support a characteristic subtype of persistent AF, critically defined by specific clinical and electrophysiological criteria. It is well recognized that persistent AF induces specific alterations in the atrial substrate potentially based on a so-called “second factor” [18,24]. However, patients with termination directly to SR, which did not develop those specific substrate alterations, seem to be protected from arrhythmia-induced modifications of the electrical and structural atrial architecture. Further studies are needed to explore the pathophysiological mechanisms behind the clinical presentation of this distinct subtype of persistent AF.

**Limitations**

In the present study, the approach to determine the mean AFCL is rather complex and time-consuming and, therefore, limited in use during the clinical routine. However, the simultaneous recording and measurement of AFCL in both atria and the CS may also help to guide the routine procedure, e.g., to identify potential AF drivers outside of the LA.

Although recommended by the international expert consensus report, we did not use a blanking period in this study. However, all patients with arrhythmia recurrences within the initial 3 months after ablation also had recurrences thereafter and were offered a repeat ablation. Thus, the overall outcome would not have been different had a 3 month blanking period been applied.
**Conclusions**

Patients with persistent AF who terminate directly to SR through ablation without the occurrence of an intermediate AT are characterized by distinct epidemiological and electrophysiological features. These distinct characteristics may indicate a specific sub-population of persistent AF patients. On multivariate analysis, only baseline AFCL emerged as a sole independent predictor of a substrate for consecutive AT.

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**Conflict of Interest Disclosures:** None

**References**


Table 1: Procedure-related data. (RF = radiofrequency).

<table>
<thead>
<tr>
<th></th>
<th>SRterm patients</th>
<th>ATterm patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td>40</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Procedure duration (min)</td>
<td>181 ± 41</td>
<td>223 ± 65</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fluroscopy time (min)</td>
<td>47 ± 19</td>
<td>63 ± 24</td>
<td>0.005</td>
</tr>
<tr>
<td>Total RF duration (sec)</td>
<td>4247 ± 1281</td>
<td>6108 ± 1485</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>RF duration until AF term. (sec)</td>
<td>4247 ± 1281</td>
<td>4447 ± 1183</td>
<td>0.237</td>
</tr>
</tbody>
</table>
**Table 2:** Patients’ baseline characteristics. (AF = atrial fibrillation, CL = cycle length, LA = left atrium, LVEF = left ventricular ejection fraction).

<table>
<thead>
<tr>
<th></th>
<th>SRterm patients</th>
<th>ATterm patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>56 ± 10</td>
<td>63 ± 9</td>
<td>0.001</td>
</tr>
<tr>
<td>AF duration (months) [Median]</td>
<td>9 ± 26 [1]</td>
<td>14 ± 20 [8]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AF history (months)</td>
<td>64 ± 52</td>
<td>82 ± 61</td>
<td>0.123</td>
</tr>
<tr>
<td>Initial AFCL (ms)</td>
<td>178 ± 23</td>
<td>159 ± 31</td>
<td>0.005</td>
</tr>
<tr>
<td>Number of previous cardioversions</td>
<td>1.3 ± 1.3</td>
<td>1.9 ± 1.4</td>
<td>0.024</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>41 ± 5</td>
<td>45 ± 5</td>
<td>0.015</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>63 ± 9</td>
<td>60 ± 14</td>
<td>0.527</td>
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</tbody>
</table>

**Table 3:** Termination sites of persistent AF resulting in conversion to AT. (LAA = left atrial appendage, RAA = right atrial appendage, CS = coronary sinus, LIPV = left inferior pulmonary vein).

<table>
<thead>
<tr>
<th>Left atrium (n = 32)</th>
<th>Right atrium (n = 16)</th>
<th>Coronary sinus (n = 5)</th>
<th>Pulmonary veins (n = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roof</td>
<td>8</td>
<td>RAA (ant)</td>
<td>7</td>
</tr>
<tr>
<td>Anterior</td>
<td>5</td>
<td>Septum</td>
<td>6</td>
</tr>
<tr>
<td>Septum</td>
<td>5</td>
<td>RA Isthmus</td>
<td>3</td>
</tr>
<tr>
<td>Inferior</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAA</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>2</td>
<td></td>
<td></td>
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</tbody>
</table>

**Table 4:** Predictors of direct termination to SR. (AFCL = atrial fibrillation cycle length, SR = sinus rhythm, AF = atrial fibrillation, LA = left atrium).

<table>
<thead>
<tr>
<th>Baseline Variable</th>
<th>p value</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
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<tr>
<td><strong>Univariate predictors of direct termination to SR</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Baseline AFCL (ms)</td>
<td>&lt;0.001</td>
<td>1.066</td>
<td>1.037 - 1.096</td>
</tr>
<tr>
<td>LA size (mm)</td>
<td>0.023</td>
<td>0.857</td>
<td>0.751 - 0.979</td>
</tr>
<tr>
<td>Number of cardioversions</td>
<td>0.033</td>
<td>0.687</td>
<td>0.486 - 0.971</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.073</td>
<td>0.943</td>
<td>0.885 - 1.005</td>
</tr>
<tr>
<td>AF duration (months)</td>
<td>0.615</td>
<td>0.996</td>
<td>0.980 - 1.012</td>
</tr>
<tr>
<td><strong>Multivariate predictor of direct termination to SR</strong></td>
<td>0.005</td>
<td>1.110</td>
<td>1.032 - 1.193</td>
</tr>
</tbody>
</table>
Figure Legends:

**Figure 1** - Termination sites leading to direct SR restoration (black stars) and conversion to AT (red dots).

**Figure 2 A-C** - Intracardiac Electrograms and Surface ECG of Termination of Atrial Fibrillation directly to Sinus Rhythm. A) Pre-ablation signals at the site of AF termination (LA roof). The local signal on the mapping catheter displays continuous high-frequency fractionation and a short AFCL. During ablation (B), AFCL lengthens but of particular note, the AF activity at the ablation site drives the rest of the atria as indicated by the slower AFCL and pause in the CS and HRA. This culminates in loss of local fractionation with further increase in AFCL prior to AF termination to SR (C).

**Figure 3 A-C** - Intracardiac Electrograms and Surface ECG of Termination of Atrial Fibrillation to Atrial Tachycardia. A) The point of AF termination during ablation at the anterior LA to an AT (CL 200 ms) is marked with a black arrow. During continued ablation at this location, AT cycle length increased from 200 to 300 ms (B). This tachycardia was ablated at the CS ostium resulting in a subsequent AT of 340 ms CL which was mapped and ablated to SR at the LA roof (C). The Lasso catheter is placed in the LAA.

**Figure 4** - Procedural outcome of both patient groups with regard to AF, AT and SR.
Atrial Fibrillation Cycle Length Is a Sole Independent Predictor of a Substrate for Consecutive Arrhythmias in Patients with Persistent Atrial Fibrillation

Imke Drewitz, Stephan Willems, Tushar V. Salukhe, Daniel Steven, Boris A. Hoffmann, Helge Servatius, Karsten Bock, Muhammet A. Aydin, Karl Wegscheider, Thomas Meinertz and Thomas Rostock

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