Quantitative Analysis of Isolation Area and Rhythm Outcome in Patients With Paroxysmal Atrial Fibrillation After Circumferential Pulmonary Vein Antrum Isolation Using the Pace-and-Ablate Technique

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Background—We sought to determine the relationship between the size of the left atrial isolated surface area (ISA) after pulmonary vein antrum isolation for paroxysmal atrial fibrillation (AF) and rhythm outcome during a 12-month follow-up.

Methods and Results—One hundred one consecutive patients with paroxysmal AF (mean age, 59±11 years; median [range] AF history, 36 [24–96] months; mean left atrial size, 42±6 mm) were enrolled. The ISA was defined as the ratio of the total isolated antral surface area excluding the pulmonary veins to the sum of the total isolated antral surface area and the left atrial posterior wall surface area, while considering the individual characteristics of antral anatomy. All surface areas were assessed using the NavX system. Patients were divided into 4 groups according to ISA (group I: <50%; group II: 50 to <60%; group III: 60 to <70%; group IV: ≥70%). The average ISA for all patients was 59.2±11.6%. Subgroup analysis showed that ISA was 42.8±4.2% in group I (n=23), 54.2±3.0% in group II (n=23), 64.3±3.0% in group III (n=33), and 73.9±3.6% in group IV (n=22). After a 12-month follow-up period, 70% of patients in group I, 78% in group II, 97% in group III, and 100% in group IV were free from AF and atrial macroreentrant tachycardia. There was a significant difference between groups I and III, I and IV, II and III, and II and IV but not groups I and II and groups III and IV (log-rank test \( P = 0.024, 0.016, 0.037, 0.044, 0.584, \) and 0.500, respectively). Receiver operating characteristic curve analysis yielded an optimal cutoff value of 55% for ISA.

Conclusions—After 12 months, a larger ISA was associated with a significantly lower AF and macroreentrant tachycardia recurrence rate. \( ISA \geq 55\% \) may thus serve as a predictor for long-term success after pulmonary vein antrum isolation. (Circ Arrhythm Electrophysiol. 2012;5:667-675.)

Key Words: ablation ■ pulmonary vein isolation ■ cardiac imaging ■ isolation area ■ rhythm outcome

Catheter ablation is a potentially curative treatment option for patients with atrial fibrillation (AF), especially for patients with paroxysmal AF.\(^1\)\(^-\)\(^3\) During the past 2 decades, the procedure has evolved from the ablation of focal AF triggers inside the pulmonary veins (PVs) to wide-area circumferential PV antrum isolation (PVAI).\(^4\)\(^-\)\(^5\) A wide ablation line encircling the entire PV antrum from the left atrial side targets both AF triggers and the perpetuating substrate. Of the various catheter ablation techniques available, PVAI is associated with a better rhythm outcome than segmental PVI for patients with paroxysmal AF.\(^6\)\(^-\)\(^8\) The reported recurrence rate after PVAI varies depending on the type of AF, the concept of lesion, the experience of the operator, the type of technical equipment, and the quality of the follow-up. However, data concerning the impact of the isolated surface area (ISA) on ablation success are limited,\(^9\) especially after PVAI using the pace-and-ablate technique. The concept of this technique is to allow the physician to easily create long left atrium ablation lines and detect residual lesion gaps. We believe that with this technique we can create wider circle lesions around ipsilateral veins. We hypothesized that the size of the ISA after PVAI correlates positively with the rate of AF and macroreentrant tachycardia (MRT) recurrences. The primary goal of this study was to determine whether ISA predicts the individual rhythm outcome for patients with paroxysmal AF after a single PVAI procedure. The secondary goal was to identify the ISA cutoff, providing sufficient sensitivity and specificity with respect to long-term success after PVAI.
Methods

Patient Selection
The study was conducted on 101 consecutive patients with highly symptomatic, medically refractory paroxysmal AF, who had been treated with PVAI between January and December 2009. Paroxysmal AF was defined as a self-terminating AF of <1 week duration.

Mapping and Ablation Procedure
Before the procedure, transoesophageal echocardiography was performed to exclude thrombus formation. Patients were studied under deep propofol sedation, breathing spontaneously. Standard electrode catheters were placed in the right ventricular apex and the coronary sinus, after which a single transseptal puncture was made. Unfractionated heparin was administered in bolus form immediately after the transseptal puncture to maintain an activated clotting time of >250 s. If AF occurred an external electrical cardioversion was performed to restore sinus rhythm. Mapping and ablation were performed using the NavX system (St. Jude Medical, Inc, St. Paul, MI) as a guide after integration of a 3-dimensional model of the left atrium (LA) and PV anatomy obtained from preinterventional computed tomography (CT), as described previously.15 Before the ablation, the circular mapping catheter–reconstructed PV anatomic images were aligned with the CT-PVs. Furthermore, the multipolar mapping catheter was replaced by a 4-mm M-curve irrigated tip ablation catheter (Balt Cooled Path, St. Jude Medical, Inc). Fine adjustment of image integration was achieved through 3 additional landmarks (at the LA roof, in the basal posterior LA, and in the LA isthmus), with the tip of the ablation catheter visiting the landmarks according to fluoroscopy and electrogram information. Integration quality assessment through 31 LA control points revealed concordance of CT surface with the true catheter tip position in 90% (84%–100%) of the control points. Ablation points were marked as a 3-dimensional Lesion on EnGuide to document the true 3-dimensional localization of the catheter tip (no projection on CT surface and no Lesion at Mouse). The true position of the catheter tip on the CT surface can be appreciated for all ablation target areas, underlying registration accuracy. Radiofrequency (RF) alternating current was delivered in a unipolar mode between the irrigated tip electrode of the ablation catheter and an external back-plane electrode. The initial RF generator setting consisted of an upper catheter tip temperature of 48°C, a maximal RF power of 40 W, and an irrigation flow rate of 30 mL/min. All patients underwent PVAI. The level of ablation was chosen at the atrial side of the PV anatomic area from the initial circumferential ablation line and especially at the carina region. The minimum time at 1 spot was 20 s for all operators. RF energy was routinely reduced by 10 W when ablat- ing the posterior wall according to the intraesophageal temperature measured with an intraluminal probe (SensiTherm, St. Jude Medical, Inc). In case the intraesophageal temperature rose above 40.0°C, ablation was immediately stopped and energy further reduced. If ablation could not be performed with 20 W, the line placement was performed either more antral or closer to the PV, depending on individual anatomic findings.11 Catheter navigation was performed with a steerable sheath (Agilis, St. Jude Medical, Inc).12 All patients with a temperature rise >40°C underwent esophagoscopy on the following day. The patients received proton pump inhibitors for 4 weeks, and esophagoscopy was repeated after 3 to 4 days if mucosal ulcerations >10 mm were initially observed.11

Ablation Line Concept and Procedural End Point
Wide ablation lines were placed to encircle the ipsilateral PVs at the antral level for PV isolation and substrate modification, guided by 3-dimensional mapping, fluoroscopy, tactile catheter feedback, impedance changes, and electrogram characteristics. The anterior line was ablated with the pace-and-ablate approach. The ridge was ablated not from the LAA side but rather from the PV side. The potentials on the spiral catheter in the left superior PV were identified as far-field signals by pacing the coronary sinus and measuring conduction times of coronary sinus–left superior PV with differential pacing. The procedural end point was considered to be the electrophysiologically proven bidirectional block for the PV-encircling ablation lines confirmed with a circular mapping catheter (Optima, St. Jude Medical, Inc). Gaps in the ablation lines were detected and closed by using the pace-and-ablate approach.14 Before the postprocedural PV assessment, a 20-minute waiting time was given for each PV-encircling ablation line to monitor for early PV reconnection. After proving the bidirectional block of the PV, we performed a stimulation protocol (burst pacing from coronary sinus with 300, 250, and 200 ms for 10 s each) for testing inducibility. When AF was induced, patients were cardioverted and the procedure ended. No pharmacological identification of non-PV triggers was performed. Ablation of the cavotricuspid isthmus was performed only if the typical right atrial flutter was either documented previously or induced by burst pacing at the end of the procedure.

Measurement and Definition of ISA
ISA was defined as the ratio of the total isolated antral surface area (IASA) excluding the PVs to the total sum of the IASA and the LA posterior wall surface area. Thus:

\[
\text{ISA} \times 100 = \text{Total IASA [cm}^2]/\text{total IASA [cm}^2]+\text{LA posterior wall surface area [cm}^2]\times 100
\]

Each of the parameters in this equation was assessed according to the following method and the use of a specific software tool of the NavX system. The NavX system automatically calculates the distal surface area from manually selected points. For instance, for calculating the surface area of PV, we must manually define the PV ostium so that NavX can perform calculation.

First, the PV ostium was defined as the point of maximal inflection between the PV wall and the LA wall. The NavX system displays the LA geometry with different angles; therefore, in a case where PV os- tium was unclear, we defined it relying on the shadow between the PV wall and the LA wall. Patients with a common trunk, we defined the second branch of common trunk as PV ostium. Second, the area between each encircling ablation line represented by the red 3-di- mensional points (Figure 1A) and the corresponding PV ostium was defined as the IASA (Figure 1B and ID). Third, the total IASA was defined as the sum of the right-sided and left-sided IASA. The LA posterior wall surface area was defined as the area delineated by the upper and lower line, connecting the most superior and inferior as- pects of the circumferential ablation lines, respectively, and the post- erior sections of the circular ablation lines (Figure 1C). Patients were divided into 4 groups according to their ISA (group I: <50%; group II: 50 to <60%; group III: 60 to <70%; group IV: ≥70%). IASA and ISA were defined as the initial attempted ablation line. Even when bidirectional block could not be achieved, despite the larger circumferential ablation with ISA of 70%, and additional point ablation at the carina region and more distal region was attempted, the patient was categorized to group IV. With the NavX system, we measured simple distances between the ablation line and PV ostium in 8 differ- ent segments (LP, left-side posterior wall; left-side inferior wall; LA, left-side anterior wall; left-side superior wall; RP, right-side posterior wall; right-side inferior wall; right-side anterior wall; right-side super- ior wall) (Figure 2). The relationship among simple distances, IASA, and ISA was compared.

Inter- and Intravariability in Measurement of IASA and ISA
To assess inter- and intraserver variability, ISA and left-sided and right-sided IASA were independently assessed by 2 experienced electrophysiologists. One of the 2 electrophysiologists evaluated the patients again 2 weeks after the initial assessment. The electrophysiologists were blinded to the results of the initial measurement and clinical outcome of 15 patients.

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Postinterventional Management and Follow-Up

Antiarrhythmic treatment was discontinued after the intervention, and a β-blocker was administered to all patients. Patients were put on oral anticoagulation for ≥6 months (target international normalized ratio, 2.0–3.0), depending on the individual stroke risk based on the CHADS2 score. Serial 7-day Holter ECGs (Lifecard CF; DelmarReynolds Medical Inc, Irvine, CA) were performed immediately after the procedure and after 3, 6, and 12 months for all patients. If symptoms occurred outside the recording period, patients were requested to contact our institution or the referring physician to obtain ECG documentation. AF and MRT episodes lasting >30 s were considered recurrences.

Statistics

The data were tested with the Kolmogorov-Smirnov test and are presented as mean±SD for normally distributed variables. Median and quartiles are given for non-normally distributed variables. Categorical variables are expressed as number and percentage of patients. Cox proportional hazards regression models were used to estimate hazard ratios and 95% CIs for AF/MRT recurrence. Variables in the multivariable Cox proportional hazards regression model included left ventricular ejection fraction, ISA, left- and right-sided IASA, and presence of left common PV with \( P < 0.05 \) using unadjusted Cox proportional hazard regression analysis. Continuous variables grouped by ISA were compared by means of 1-way ANOVA and post hoc analysis with Bonferroni correction for multiple comparisons of data, if normally distributed, or the Kruskal-Wallis test, if skewed. Categorical variables were analyzed with the Fisher exact test. Receiver operating characteristic curves were used to determine the ISA that provided the best sensitivity and specificity for elimination of AF and MRT after a single PVI procedure. Specificity rather than sensitivity was prioritized in optimality estimation with receiver operating characteristic analysis. With regard to the relative costs of false-positive and false-negative results, false positive <10%, indicating AF and MRT recurrences despite ISA greater than a cutoff value, was considered an optimal cutoff for ISA. Freedom from AF and MRT was determined with the Kaplan-Meier method. Survival analysis grouped by ISA was performed using log-rank test and post hoc analysis using the Holm method. The statistical α error limit of ≤5% was considered to be acceptable. Using a linear regression model, we evaluated inter- and intraobserver variability in estimating ISA and left- and right-sided IASA. Categorical analyses were performed with SPSS, release 11.0.

Results

Patient Characteristics

Patient characteristics are displayed in Table 1. A total of 101 patients with symptomatic paroxysmal AF and a median...
AF history of 36 (first to third quartile, 24–96) months were included in this study. Their mean age was 59±10 years, and 72 patients (71%) were men; the mean LA diameter was 42±6 mm and the left ventricular ejection fraction was 61±7%. Hypertension was present in 60 (59%) and coronary artery disease in 16 patients (16%). Ablation of the cavotricuspid isthmus had been previously performed in 12 patients (12%).

Ablation Procedure Results
Ablation was performed by 5 experienced electrophysiologists. Complete PVAI could be achieved in all patients. The mean procedure time was 142±44 minutes, mean fluoroscopy time was 36±15 minutes, and median RF burning time was 34 (range, 28–46) minutes. Unadjusted Cox proportional hazard regression analysis revealed no statistically significant differences in parameters between patients with and without arrhythmia recurrences (Table 2). One patient suffered a pericardial tamponade requiring pericardiocentesis, but no other major complications were observed during the procedure and the follow-up period.

Size and Distribution of IASA, ISA, and Simple Distances
Fifteen patients (15%) had a left common PV and 7 patients (7%) a right middle PV. Variations in both the LA and PV anatomy were evenly well divided between patients with and without arrhythmia recurrences.

The mean ISA measured 59.2±11.6% and the mean IASA of the left antrum was 9.0±4.3 cm² and that of the right antrum was 11.0±4.5 cm² (Figure 3). Unadjusted Cox proportional hazard regression analysis identified 4 factors related to AF and MRT recurrences: low left ventricular ejection fraction, presence of left common PV, small left- and right-sided IASA, and small ISA (Table 2). The duration of AF history, lone AF, left atrial diameter, and flow velocity of left atrial appendage were not associated with AF and MRT recurrences. According to the multivariable Cox proportional hazard regression analysis, the most predictive model of AF and MRT recurrences consisted of small ISA. Figure 4 shows 2 representative examples of a larger and a smaller area of PVAI.

As for simple distances between ablation line and PV ostium, mean LP, left-side inferior wall, LA, left-side superior

Table 2. Cox Regression Analysis of Preprocedural and Procedural Characteristics in Association With AF/MRT Recurrence

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted HR</th>
<th>95% CI</th>
<th>P</th>
<th>Adjusted HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>1.03</td>
<td>0.97–1.10</td>
<td>0.33</td>
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<tr>
<td>Male, n (%)</td>
<td>2.26</td>
<td>0.76–6.73</td>
<td>0.14</td>
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<tr>
<td>AF history, mo</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.86</td>
<td></td>
<td></td>
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<tr>
<td>Antiarrhythmic drugs, n</td>
<td>1.10</td>
<td>0.38–2.99</td>
<td>0.90</td>
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<tr>
<td>Arterial hypertension, n (%)</td>
<td>1.52</td>
<td>0.47–4.94</td>
<td>0.48</td>
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<tr>
<td>Coronary artery disease, n (%)</td>
<td>1.60</td>
<td>0.44–5.80</td>
<td>0.48</td>
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<tr>
<td>Diabetes mellitus, n (%)</td>
<td>1.54</td>
<td>0.20–11.87</td>
<td>0.78</td>
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<tr>
<td>Lone AF, n (%)</td>
<td>0.78</td>
<td>0.24–2.55</td>
<td>0.84</td>
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<tr>
<td>Left atrial diameter, mm</td>
<td>0.96</td>
<td>0.87–1.10</td>
<td>0.96</td>
<td></td>
<td></td>
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<tr>
<td>Flow velocity in LAA, cm/s</td>
<td>0.98</td>
<td>0.94–1.01</td>
<td>0.18</td>
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<tr>
<td>LV ejection fraction, %</td>
<td>0.92</td>
<td>0.86–1.00</td>
<td>0.05</td>
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<td>Prior CTI ablation, n (%)</td>
<td>0.74</td>
<td>0.17–3.50</td>
<td>0.74</td>
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<tr>
<td>ISA, %</td>
<td>0.89</td>
<td>0.84–0.94</td>
<td>0.001</td>
<td>0.89</td>
<td>0.84–0.94</td>
<td>0.001</td>
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<tr>
<td>Left-sided IASA, cm²</td>
<td>0.79</td>
<td>0.66–0.96</td>
<td>0.015</td>
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<tr>
<td>Right-sided IASA, cm²</td>
<td>0.82</td>
<td>0.69–0.98</td>
<td>0.025</td>
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<tr>
<td>Procedure time, min</td>
<td>0.99</td>
<td>0.97–1.00</td>
<td>0.15</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fluoroscopy time, min</td>
<td>1.01</td>
<td>0.97–1.04</td>
<td>0.66</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RF burning time, min</td>
<td>1.00</td>
<td>1.00–1.00</td>
<td>0.86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left common pulmonary vein, n (%)</td>
<td>0.24</td>
<td>0.08–0.72</td>
<td>0.01</td>
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<tr>
<td>Right middle pulmonary vein, n (%)</td>
<td>0.88</td>
<td>0.12–6.80</td>
<td>0.90</td>
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</table>

AF indicates atrial fibrillation; MRT, macroreentrant tachycardia; LAA, left atrial appendage; LV, left ventricular; CTI, cavotricuspid isthmus; RF, radiofrequency; ISA, isolated surface area; IASA, isolated antral surface area.
wall, RP, right-side inferior wall, right-side anterior wall, and right-side superior wall were measured as 10.5±4.5, 4.4±2.2, 3.3±1.4, 6.1±3.6, 9.7±4.3, 3.8±2.2, 6.5±3.7, and 4.8±2.8, respectively. LP and RP were statistically correlated with left- and right-sided IASA, respectively (r=0.78, P<0.001; and r=0.77, P<0.001, respectively). In groups III and IV, the mean LP was measured as 11.6±2.7 and 15.0±5.0 mm, respectively. The mean RP was measured as 11.5±3.0 and 13.3±4.6 mm, respectively. Interestingly, the total sum of LP and RP was also correlated with ISA (r=0.75, P<0.001) (Figure 5).

Inter- and Intravariability in Measurement of IASA and ISA
When estimating the left- and right-sided IASA and the ISA, there was excellent correlation between electrophysiologist 1 and electrophysiologist 2, as well as the initial and the second calculation (in interobserver, respectively: r=0.97, P<0.001; r=0.96, P<0.001; r=0.85, P<0.001; in intraobserver, respectively: r=0.99, P<0.001; r=0.99, P<0.001; r=0.97, P<0.001) (Figure 6). This suggested that both inter- and intraobserver variability were within an acceptable range.

IASA and Procedural Data for Patients Grouped by ISA
Table 3 shows IASA and procedural data for patients grouped according to ISA. Groups I and II comprised 23 patients (23%) each, group III 33 (33%) patients, and group IV 22 (22%) patients. ISA was 42.8±4.2% for group I, 54.2±3.0% for group II, 64.3±3.0% for group III, and 73.9±3.6% for group IV. Left-sided IASA showed significant differences between and among all groups except for groups II and III (P=1.0). It is noteworthy that there were no significant differences in LA size, abnormality of PV anatomy, esophageal course, and procedural complexity between and among the groups (Table 3).

Rhythm Outcome and Size of ISA
After a mean follow-up period of 12±3 months, AF and MRT recurrences were observed in 13 patients (13%) after a single PVAI procedure without concomitant antiarrhythmic treatment. Kaplan-Meier curve revealed that freedom from AF and MRT recurrences at 12 months after a single procedure with PVI was 70% in group I, 76% in group II, 97% in group III, and 100% in group IV. Among all 4 groups, there was a significant difference in AF and MRT recurrences (log-rank test, P=0.003). The pair-wise comparison by Holm-corrected threshold demonstrated significant differences between groups I and III, I and IV, II and III, and II and IV but not groups I and II and groups III and IV (0.024, 0.016, 0.037, 0.044, 0.584, and 0.500, respectively) (Figure 7). Receiver operating characteristic curve analysis yielded the optimal cutoff value of 55% for ISA. The sensitivity, specificity, and positive and negative predictive values for cutoff values are shown in Table 4.

Discussion
Main Findings of the Study
The study presented here demonstrates that ISA is associated with a recurrence of AF and MRT after a single PVAI procedure. PVAI is reportedly a more effective treatment for AF than isolation of individual PVs. However, there have been few reports on predictors of AF recurrence after a single PVAI procedure for patients with paroxysmal AF. Therefore, with the first goal of our study to investigate whether ISA is associated with AF and MRT recurrences, we concluded by means of multivariable analysis that ISA was the only predictor.

The second goal was to determine the optimal cutoff value of ISA. During a 12-month follow-up after a single PVAI procedure, the recurrence rate was low in groups III and IV (ISA≥60%). According to receiver operating characteristic curve analysis, the optimal cutoff value of ISA was 55%, with excellent specificity and positive predictive value for elimination of AF and MRT.

Predictor of Recurrence After 12-Month Follow-Up
Patients with paroxysmal AF showed a high clinical success rate, with only 13% suffering from AF and MRT recurrences after the 12-month follow-up. A Cox multivariable hazard
regression analysis performed during follow-up indicated that only ISA was associated with AF and MRT recurrences. Previous studies have reported that hypertension, duration of AF, LA volume, and PV anatomy could predict recurrence in patients with paroxysmal and persistent AF. However, in our study, those parameters could not be associated with recurrence. The reason for this discrepancy may be related to the type of AF because only patients with paroxysmal AF were enrolled. In addition, a multivariable analysis was performed with a multiple logistic analysis in most of the studies. No survival analysis was performed.

Distribution of ISA
ISA data showed a normal distribution but varied among patients. Our ablation line concept consisted of a previously reported single method. Wide circumferential ablation lines placed from the LA side around the opening of the PV antrum are considered the basis for treatment of patients with paroxysmal and persistent AF.

Table 3. Clinical Outcomes, Abnormality of PV, Size of LA, Esophageal Course, and Procedural Data for Patients Grouped by ISA

<table>
<thead>
<tr>
<th>ISA, %</th>
<th>Group I (n=23)</th>
<th>Group II (n=23)</th>
<th>Group III (n=33)</th>
<th>Group IV (n=22)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>59.2±11.6</td>
<td>42.8±4.2</td>
<td>54.2±3.0</td>
<td>64.3±3.0</td>
<td>73.9±3.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>9.0±4.3</td>
<td>5.5±2.6</td>
<td>7.1±2.3</td>
<td>10.0±3.0</td>
<td>13.3±4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>11.0±4.5</td>
<td>6.5±1.6</td>
<td>9.6±2.7</td>
<td>12.9±4.8</td>
<td>14.1±3.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>42±6</td>
<td>41±7</td>
<td>42±5</td>
<td>43±6</td>
<td>43±6</td>
<td>NS (0.57)</td>
</tr>
<tr>
<td>15 (15)</td>
<td>6 (26)</td>
<td>2 (8)</td>
<td>5 (15)</td>
<td>2 (9)</td>
<td>NS (0.38)</td>
</tr>
<tr>
<td>7 (7)</td>
<td>1 (4)</td>
<td>2 (8)</td>
<td>1 (3)</td>
<td>3 (14)</td>
<td>NS (0.49)</td>
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</tbody>
</table>

Esophageal course

<table>
<thead>
<tr>
<th>ISA, %</th>
<th>Group I (n=23)</th>
<th>Group II (n=23)</th>
<th>Group III (n=33)</th>
<th>Group IV (n=22)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>50 (50)</td>
<td>11 (48)</td>
<td>14 (61)</td>
<td>15 (46)</td>
<td>10 (45)</td>
<td>NS (0.67)</td>
</tr>
<tr>
<td>35 (35)</td>
<td>9 (39)</td>
<td>4 (17)</td>
<td>12 (36)</td>
<td>10 (45)</td>
<td>NS (0.21)</td>
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<tr>
<td>16 (16)</td>
<td>3 (13)</td>
<td>5 (22)</td>
<td>6 (18)</td>
<td>2 (9)</td>
<td>NS (0.69)</td>
</tr>
<tr>
<td>142±44</td>
<td>144±53</td>
<td>145±55</td>
<td>145±51</td>
<td>133±42</td>
<td>NS (0.79)</td>
</tr>
<tr>
<td>38±16</td>
<td>40±21</td>
<td>33±11</td>
<td>33±10</td>
<td>32±11</td>
<td>NS (0.22)</td>
</tr>
<tr>
<td>34 (28–46)</td>
<td>34 (30–41)</td>
<td>35 (28–60)</td>
<td>34 (26–46)</td>
<td>30 (28–45)</td>
<td>NS (0.38)</td>
</tr>
</tbody>
</table>

Recurrence of AF/MRT, n (%) 13 (15) 7 (30) 5 (21) 1 (3) 0 (0)
Recurrence of AF only, n (%) 7 (30) 1 (4)
Recurrence of MRT only, n (%) 1 (4) 1 (3)
Recurrence of AF and MRT, n (%) 3 (13)

ISA indicates isolated surface area; IASA, isolated antral surface area; LA, left atrium; RF, radiofrequency energy; AF, atrial fibrillation; MRT, macroreentrant tachycardia.
However, continuity and transmurality of these lesions are difficult to achieve because of individually variable and complex LA anatomy. Furthermore, selection of the posterior line was limited because of the increase in the temperature of the esophagus, the variability of anatomy of antrum and PV, and difficulty of ablation catheter placement around the antrum. These factors may account for the differences in ISA among patients. The anatomy of LA may be slightly more complex or the temperature increase of the esophagus more severe in groups I and II than in groups III and IV.

Quantitative Analysis of ISA and Rhythm Outcome

We attempted a precise and objective assessment of the clinical outcome with serial 7-day Holter ECGs to assess not only the rate of AF recurrences but also the rate of secondary arrhythmias, such as MRT, which are clinically just as relevant as AF. Previous studies have reported that most AF recurrences occur within 6 to 10 months of the index ablation and that PV reconduction is one of the most common mechanisms of arrhythmia recurrence. All 13 patients in this study showed recurrence of AF and MRT within 10 months after a single PV AI procedure. Five (38%) had PV reconduction, 7 (54%) had relatively distally isolated PVs, and 1 (8%) had no PV reconduction at all. Interestingly, 11 of the patients (85%) had ISA<55%. In 7 patients with ISA<50%, the recurrence was only AF, whereas in 2 patients with ISA>55% the recurrence was only MRT (ISA, 57% and 62%) (Table 3). In the second session, in those 2 patients, the PV-LA was distally isolated and reconducted in the antral area, which was ablated in the first session. We suspected that the distal isolation in patients with larger ISA was possibly caused by the procedure in which we first attempted a wider isolation line and then had to change to a smaller isolation because of difficulties in achieving complete PVAI. This suggests that the substrate with an incomplete larger circular lesion or reconduction of a larger circular lesion might be the cause of MRT recurrence but not AF recurrence. We often detected LA capture at the antral region even if there was no PV reconduction. In addition to PV reconduction, the main mechanism of recurrence in our study was considered to be a residual substrate in the PV antrum. Arentz et al reported that the recurrence rate after a follow-up period of 15±6 months was significantly lower in the group with PV AIs than in those who underwent individual PVI. The authors performed PV AI on the posterior wall >10 mm from the PV ostium. In our study, the mean LP and RP were measured as 12±4 and 11±4 mm for patients with ISA≥55, which was somewhat longer than their PV AI. Because our success rate was considerably better than in previous reports, it seems that a relatively wide PV AI is advisable to cure patients with AF. Simply, circumferential ablation with a minimum distance of 12 mm from the PV ostium is recommendable to achieve ISA≥55%.

Mechanism of AF and MRT Recurrences and Clinical Implication

Previous studies have reported that the mechanisms of recurrence of AF are (1) primarily incomplete PV antrum isolation, (2) distally isolated PVs, (3) a high incidence of PV reconduction, and (4) non-PV foci. We achieved success with a single PVI procedure in terms of freedom from AF and MRT for >80% of our patients, which is a high success rate among related studies to date. Furthermore, in the groups with a large PV AI (groups III and IV), only 1 of 55 patients...
(1.8%) suffered from AF recurrence. This suggests that the atrial myocardium around PVs is involved in the pathophysiology of AF because PV foci, autonomic ganglia around PVs, and arrhythmogenic substrate have been observed in this area around PVs.

Because previous studies have reported that the anatomic distribution of areas with maximum ganglionated plexi (GP) was located near the PV ostium,27,28 GP ablation was performed in areas at a minimal distance from the PV ostium (5–10 mm). The size of the ablated area ranged from 1.4±0.8 to 2.2±1.5 cm.29 Using this parameter, the GP ablation area can be calculated as ≈2.6 cm². Our ablation area with a large PVAI, total IASA, is 11.5±3.9 cm² in group III and 13.7±4.1 cm² in group IV, which seems to be larger than the GP ablation area. Another study reported that addition of anatomic GP modification to PV isolation yields significantly better outcomes than PV isolation alone during a follow-up period of 12 months.29 The reported success rate was 85.3%, similar to ours.

As for non-PV foci, a previous study reported that 26% of patients with paroxysmal AF possess non-PV foci and that the LA roof was one of the most prevalent sites of non-PV foci.25 In another study, the majority of foci were located proximally in group IV, which seems to be larger than the GP ablation area. We recommend that, in addition to the impact of PV isolation, an ablation line with a large PVAI might affect autonomic ganglia around PVs and non-PV foci around the PV antrum.

Study Limitations

Our study has 2 major limitations. First, the sample size was rather small. Second, this study was nonrandomized and not designed to clearly compare procedural outcomes with those obtained using other methods. Our findings should, therefore, be verified in a randomized prospective study.

Conclusions

Patients free from AF and MRT after treatment with a single PVAI procedure were found to have a larger ISA. This indicates that ISA≥55% can serve as a predictor for long-term success after PVAI. Based on our experience, we recommend that when treating AF, despite the complex anatomy and individual variables of the PV antrum, physicians should attempt to establish a wide ablation line encircling the entire PV antrum from the left atrial side.

Acknowledgments

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Disclosures

C.P. has received modest lecture honoraria from St. Jude Medical and Biotronik and is a member of the St. Jude Medical advisory board. S.R., P.S., T.G., and A.A. have received modest lecture honoraria and congress sponsoring from St. Jude Medical and Biosense. G. H. has received modest lecture honoraria from St. Jude Medical, Biotronik, Medtronic, and Biosense and is a member of the St. Jude Medical and Biosense advisory boards. The other authors have no conflicts to report.

References

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CLINICAL PERSPECTIVE

Atrial fibrillation catheter ablation is now a routine procedure with wide circumferential pulmonary vein isolation as the cornerstone. However, the quantitative analysis of isolation area has not been well discussed. We calculated the isolated surface area using the commercially available NavX system. Our study demonstrated that wider circumferential pulmonary vein isolation with isolated surface area (ISA) ≥55% promises an excellent rhythm outcome after a single procedure compared with relatively narrow circumferential pulmonary vein isolation. Our results showed that simple distances between the ablation line and PV ostium, especially in the segments of left-side posterior wall and right-side posterior wall, were correlated with each sided isolated antral surface area. The sum of left-side posterior wall and right-side posterior wall was correlated with ISA. The question is, What is the minimum distance between wide circumferential ablation lesion sets of the right and left side? Simply, wide circumferential ablation with the minimum distance of 12 mm from PV ostium is recommendable to achieve ISA≥55%. Regarding recurrence, in patients with ISA<50% it was only atrial fibrillation, whereas in patients with ISA≥55% it was only macroreentrant tachycardia. These findings suggest that the substrate with incomplete wider circumferential lesions or reconstruction of wider circumferential lesions might be the cause of macroreentrant tachycardia recurrence but not atrial fibrillation recurrence. We believe that radiofrequency application using the pace-and-ablate technique can reduce the incomplete lesion and reconstruction, resulting in excellent rhythm outcome after a single procedure with wide circumferential pulmonary vein isolation with ISA≥55%.


Quantitative Analysis of Isolation Area and Rhythm Outcome in Patients With Paroxysmal Atrial Fibrillation After Circumferential Pulmonary Vein Antrum Isolation Using the Pace-and-Ablate Technique

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