What Is the Acute Antral Lesion Size After Pulmonary Vein Isolation Using Different Balloon Ablation Technologies?

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**Background:** Clinical outcome after pulmonary vein isolation (PVI) may be linked to both durability of PVI and the antral lesion size. Data on balloon-guided technologies are scarce. We investigated the size of the isolated surface area (ISA) acutely after PVI achieved by cryoballoon (CB) or laser balloon (LB), both using voltage mapping.

**Methods and Results:** In 40 patients (73% male, mean age 66±9 years), a bipolar voltage map before and after PVI in sinus rhythm was acquired to delineate the isolated antral surface area (IASA, contiguous area of low voltage <0.5 mV) and the ISA (relative size of the low-voltage area in relation to the whole antral surface area including the posterior wall). IASA (CB: 57±14 cm² vs. LB: 42±15 cm²; P=0.002) as well as ISA (65±8% vs. 54±10%; P=0.001) were significantly larger in the CB than in the LB group. No periprocedural complications occurred. During a mean follow-up of 326±142 days, 4/20 and 5/20 patients experienced an AF/AT recurrence in the CB and LB groups, respectively. No differences in clinical outcome were observed between patients with a large (≥55%) or small (<55%) ISA.

**Conclusions:** Balloon-guided PVI is associated with antral lesion formation. CB-guided PVI is associated with the largest ISA as compared with LB procedures. ISA size did not correlate with clinical outcome after a single procedure in the present study population.

**Key Words:** Ablation; Atrial fibrillation; Scarring; Voltage mapping

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Electrical pulmonary vein isolation (PVI) is the cornerstone of any ablation procedure for patients with paroxysmal atrial fibrillation (PAF). Patients’ clinical outcomes are predominantly determined by the durability of electrical PVI. Aside from triggered activity emanating from the myocardial PV sleeves, the complex peri-ostial atrial myocardium is deemed to contribute to the initiation and perpetuation of AF. Moreover, the antral region houses numerous ganglionated plexi and rotors potentially sustaining AF. Nonetheless, controversy exists on the value of encircling the peri-ostial tissue by wide antral circumferential ablation lines as opposed to a more distal (so-called segmental) ablation approach.

A recent study found a correlation between the area of isolated peri-ostial myocardium and clinical outcome in patients treated with irrigated radiofrequency current (RF) ablation. Although novel ablation devices such as the cryoballoon (CB; Arctic Front Advance™, Medtronic) and the laser balloon (LB; HeartLight™, CardioFocus) have shown favorable rates of acute and durable PVI, data on the area of isolated atrial antral myocardium following a balloon-based PVI approach are scarce.

We therefore investigated the size of the isolated antral surface area (IASA) as well as the isolated surface area (ISA; relative size of the low-voltage area (LVA) in relation to the whole antral surface area including the posterior wall) acutely after PVI achieved by balloon ablation devices using voltage mapping.

**Methods**

Patients aged 18–80 years with symptomatic drug-refractory paroxysmal or short-lasting persistent (<6 months episode duration) AF indicated for PVI were eligible for this study. Prior to enrolment patient informed consent was obtained. The institutional review board approved the study. Patients were excluded if they had undergone a previous PVI attempt or had a left atrial (LA) size >55 mm, valvular dysfunction >II, or a LVA prior to PVI detected by bipolar voltage mapping (see below).

**Baseline Assessment**

Transthoracic and transesophageal echocardiography was performed before the procedure in each patient in order to assess LA size, valve patency and to rule out LA thrombus.
Electrophysiological Procedure

The procedures were performed under deep sedation, using boluses of midazolam and fentanyl, as well as continuous infusion of propofol 1%. Throughout the procedure non-invasive blood pressure and oxygen saturation were continuously monitored. An esophageal temperature probe (SensiTherm™, St. Jude Medical, MN, USA) was inserted trans-orally to monitor esophageal temperature during ablation (cutoff temperature for CB 15°C and for LB or RF 39°C).

After placing 2 multipolar catheters in the coronary sinus and at the His bundle, a single transseptal puncture was performed using the modified Brockenbrough technique. An 8.5F sheath (SL1; St. Jude Medical) was advanced into the LA. Prior to transseptal puncture unfractionated heparin was administered to maintain activated clotting time ≥300 s. Selective PV angiography was performed to identify the PV ostia. A circular mapping catheter (CMC; Biosense Webster Inc., CA, USA) was placed at the PV ostium to record PV potentials through a computerized EP-system (Axiom Sensis XP, Siemens, Germany) and was then used as a roving catheter to reconstruct the LA anatomy and the baseline voltage map.

Thereafter, the single transseptal sheath was exchanged for a 12F steerable sheath.

Ablation Protocols

CB-Guided PVI  In the CB group, the “single big balloon strategy” was pursued.17 A 2nd-generation 28-mm balloon (Arctic Front Advance™, Medtronic) was introduced into the LA via the 12F steerable sheath (FlexCath™, Medtronic). Mapping of the PV was performed before, during and after freezing with an endoluminal spiral mapping catheter (Achieve™, Medtronic). Occlusion angiograms were used to obtain optimal PV occlusion and an ostial/antral balloon position. Cryoenergy was employed for 240 s at each PV followed by one “bonus” application (240 s) after successful PVI.18

LB-Guided PVI  In the LB group, the sizeable balloon (HeartLight™, CardioFocus, MA, USA) was navigated to the individual PV by the steerable sheath and inflated to obtain optimal PV occlusion. Ablation lesions were deployed in a contiguous fashion under visual guidance, titrating the energy from 5.5 to 12 W (20–30 s ablation time) according to the degree of tissue exposure. After complete visually guided circular ablation, the PVs were remapped for entrance block using the CMC. In the case of ambiguous PV recordings, differential pacing and pacing from the CMC was performed to verify PVI. In the case of residual LA-to-PV conduction, additional ablation was carried out using the LB according to the activation sequence in the CMC as recently described.19 During ablation at the right superior pulmonary vein (RSPV), diaphragmatic function was monitored by continuous pacing (12 V, 2.9 ms) of the right phrenic nerve with a 6F diagnostic catheter positioned in the superior vena cava in both balloon groups. If loss or weakening of capture was observed, energy delivery was instantly terminated.

LA Voltage Mapping  A bipolar voltage map using NavX Ensite Velocity™ (St. Jude Medical) before and after PVI in sinus rhythm was acquired. An octapolar catheter was placed in the coronary sinus to obtain a stable reference. LA geometry and peak-to-peak voltages were collected using the decapolar CMC (15 mm, with 2–5–2-mm inter-electrode spacing) as a roving catheter. The bipolar electrograms were filtered with a highpass of 30 Hz and a lowpass of 300 Hz. High-density mapping was performed along the PV ostia. After map completion, all acquired points were reassessed and manually edited offline according to predefined criteria: elimination of atrial premature beats, artifacts and far-field EGMs (Electrograms) of the LA appendage. LVAs were defined as contiguous areas of bipolar voltage amplitude ≤0.5 mV.20 Maps were automatically displayed in a color-coded fashion (grey: ≤0.5 mV; purple ≥1.0 mV). If LVAs were detected before ablation, the
The level of ablation scar was quantitatively assessed offline by measuring the LVAs using the NavX™ system. The following parameters were measured with an implemented software tool allowing for exact determination of the map’s surface area within an area of manually selected points (Figure 1). (1) The left and right isolated antral surface areas (IASA-L and IASA-R; cm²) were defined as the area of the most cranial and most caudal points of the LVA around the ipsilateral PV ostia. As a sum, the total IASA (IASA-T=IASA-L+IASA-R cm²) was calculated. (2) In order to determine the size of the non-ablated LA posterior wall area (LA PW; cm²) horizontal lines between the most cranial and most caudal points of the LVA around the PV ostia delineated the respective borders of the LA PW. The area between these lines and the posterior border of the LVAs was subsequently assessed. (3) To account for differences in the baseline ASA, the relative size of the LVA (i.e., the isolated surface (ISA) was computed using the following formula: ISA (%)=IASA-T/(IASA-T+LA PW)×100. (4) The diameters of the PV ostia were measured (mm) on PV angiography and in standard projections (RAO 30°; LA 40°).

Two independent electrophysiologists blinded to the respective technology used and blinded to each other repeated the measurements twice. Inter- and intra-observer variability was assessed thereafter. In order to assess a correlation between ISA and clinical outcome, we divided our study population into 2 groups (ISA ≥55%; ISA <55%), based on the results of a recent study that found a better prognosis in patients with a larger ISA (≥55%) after RF PVI ablation.13

Post-Procedural Care
After echocardiographic exclusion of pericardial effusion, oral anticoagulation with vitamin K antagonists or a direct anticoagulant was resumed and previously ineffective antiarrhythmic drug therapy was discontinued. For 2 weeks after the ablation, proton pump inhibitor therapy was administered. 

Follow-up
All patients were scheduled for outpatient visits including a 72-h Holter ECG at 3, 6 and 12 months. In the case of symptoms suggestive of arrhythmia recurrence, patients were equipped with an external event monitor. An AF recurrence was defined as documented AF episode lasting >30 s.12

Statistical Analysis
Statistical analysis was performed using SPSS version 20.0 for windows (SPSS Inc., IL, USA). P-values <0.05 were considered statistically significant. Continuous variables are given using mean and standard deviation or median and interquartile range where appropriate. Qualitative variables are shown as frequencies and percentages. Comparisons between groups were performed using t-test (continuous), Chi-square (categorical) and non-parametric rank test (Mann-Whitney U test).

Inter- and intra-observer variability was evaluated using a linear regression model.

To assess if ISA and the clinical success rate were linked, we divided the study population into 2 groups according to ISA size (ISA <55%; ISA ≥55%).13 and outcomes in both groups were assessed and compared by means of Chi-square analysis.

Results

Patients’ Characteristics
A total of 50 consecutive patients were enrolled in the study. Of them, 10 had to be excluded because LVAs were detected during pre-ablation mapping.

The demographics of the remaining 40 patients are given in Table 1. Most were male with a mean age of 66±9 years and in 80% of cases were scheduled for ablation because of drug-refractory PAF. The lowest prevalence of persistent AF was noted in the CB group. Echocardiography revealed normal cardiac dimensions with preserved left ventricular ejection fraction. No significant differences in baseline characteristics were observed between groups.

Mapping Results
The PV sizes were similar in both groups (Table 2), except for the RIPV. Of note, 2 patients displayed variant PV anatomy with the presence of a LCPV (n=2 in the LB group).

Table 1. Baseline Characteristics of the Study Population of Patients With AF

<table>
<thead>
<tr>
<th>Age (years), mean±SD</th>
<th>Male, n (%)</th>
<th>Persistent AF, n (%)</th>
<th>Hypertension, n (%)</th>
<th>Diabetes, n (%)</th>
<th>CAD, n (%)</th>
<th>LA (mm), mean±SD</th>
<th>LVEF (%), mean±SD</th>
<th>No. of AAD, median</th>
</tr>
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<tr>
<td>66±9</td>
<td>29 (73)</td>
<td>8 (20)</td>
<td>35 (87)</td>
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<td>8 (20)</td>
<td>40±5</td>
<td>62±4</td>
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<td>67±9</td>
<td>16 (80)</td>
<td>6 (30)</td>
<td>19 (95)</td>
<td>1 (5)</td>
<td>5 (25)</td>
<td>40±4</td>
<td>61±5</td>
<td>1 (0; 1)</td>
</tr>
<tr>
<td>66±10</td>
<td>13 (65)</td>
<td>2 (10)</td>
<td>16 (80)</td>
<td>1 (5)</td>
<td>3 (15)</td>
<td>40±5</td>
<td>63±3</td>
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<td>0.441</td>
<td>0.288</td>
<td>0.114</td>
<td>0.151</td>
<td>0.526</td>
<td>0.429</td>
<td>0.951</td>
<td>0.400</td>
<td>0.204</td>
</tr>
</tbody>
</table>

AAD, antiarrhythmic drugs; AF, atrial fibrillation; CAD, coronary artery disease; CB, cryoballoon ablation; LB, laser balloon ablation; LA, left atrium; LVEF, left ventricular ejection fraction.
Antral Lesion Size After PVI

175

The IASA-R in all groups (mean IASA-L 22±9 vs. 19±7 cm²; P=0.029; Table 3, Figures 2B,3). A significantly wider IASA-R and IASA-L were present in the CB group (IASA-R: 22±9 vs. 19±7 cm² (LB); P=0.001; IASA-L: 25±10 vs. 19±7 cm² (LB); P=0.029; Table 3, Figures 2B,3). However, the mean IASA-L was consistently smaller than the IASA-R in all groups (mean IASA-L 22±9 vs. 27±11 cm²; P=0.007). This resulted in statistically significant differences in ISA of 65±8% and 54±10% using CB and LB, respectively (P=0.001).

Figure 2. Post-ablation voltage maps after pulmonary vein isolation (PVI) using 2 different technologies. (Left) Schematic representation of the technology used for PVI (A=LB; B=CB). (Right) Post-ablation voltage maps (grey: ≤0.5 mV; purple ≥1.0 mV). The isolated area is significantly larger after CB-guided PVI. CB, cryoballoon ablation; LB, laser balloon ablation.

Figure 3. Comparison of isolated areas across the study population. All the isolated antral surface areas (right, left and total: IASA-R, IASA-L, IASA-T), as well as the isolated surface area (ISA), were significantly larger in the CB group compared with LB. CB, cryoballoon ablation; LB, laser balloon ablation.
PERROTTA L et al.

Regression Interobserver

Regression Intraobserver

Figure 4. Inter- and intra-observer variability of measurements for isolated surface area (ISA) in the 2 groups according to ablation technique used. CB, cryoballoon ablation; LB, laser balloon ablation.

Inter-Rater Variability
Linear regression analysis for ISA evaluation demonstrated excellent correlation for inter- and intra-observer variability (inter-observer, LB: r=0.93 P<0.001; CB: r=0.88, P<0.001; intra-observer, LB: r=0.93, P<0.001; CB: r=0.91, P<0.001; Figure 4).

Procedural Data
The mean procedure time, including pre- and post-ablation voltage mapping, was 122±34 min (Table 2). It was significantly higher using LB (141±31 min) as compared with CB (103±24 min; P<0.001). Mean remapping time did not differ among the groups (18±3 min). Fluoroscopy time was lower in the LB group compared with CB (12±3 vs. 14±5 min; P=0.148, trend).

No periprocedural complications were observed.

Follow-up and Repeat Interventions
During a mean follow-up of 326±142 days, 4 and 5 patients in the CB and LB groups, respectively, experienced an AF/AT recurrence. A total of 3 patients from the LB group, and one from the CB group underwent a repeat ablation.
Antral Lesion Size After PVI

procedure, PV remapping revealed a LA-to-PV reconnection in 1/12 PVs (8%) in the LB group. All the PVs were chronically isolated in the CB group.

ISA and Clinical Success Rate
Overall, 67% of the patients exhibit a large ISA (≥55%; Figure 5A) but no differences in clinical outcome were observed between patients with a large ISA (≥55%) and patients with a small ISA (<55%) (Figure 5B; P=0.952).

Discussion
The goal of the present study was to describe the acute lesion size following balloon-guided PVI using different ablation technologies. For the first time, a prospective comparative analysis was performed using post-ablation electroanatomical voltage mapping. The major findings were: (1) IASA-T was significantly larger after CB-guided PVI compared with LB; (2) this difference resulted from a larger IASA-R around the right PVs; (3) this resulted in an ISA of almost two-thirds of the total antral LA surface area using CB as compared with 54% using LB; and (4) no correlation between ISA and clinical outcome was observed during a 1-year follow-up.

Lesion Location and Differences in IASA
It has been shown in previous studies using RF that the IASA size after circumferential PVI varies substantially and that a large IASA is associated with improved clinical outcome. Previous observations have shown that balloon-guided PVI creates lesion sets outside the tubular portion of the PV but leaves the antral myocardium rather unaffected, thus being deemed to be truly ostial. This may not apply to the 28-mm 2nd-generation CB, as recently demonstrated by voltage mapping and biomarker release.

According to the present study’s results, the 2nd-generation CB enabled more proximal (i.e., antral) ablation lesions involving a large amount of atrial myocardium. These differences might be explained by the exclusive use of the 28-mm CB and the new technical design with a larger zone of cooling. On the other hand, despite the ability to inflate to a maximum of 32 mm the LB created smaller IASAs. It is speculated, that (1) the discrete ablation spots of the diode laser (30° of an arc, width 2 mm; Figure 2A) may have provided more discrete lesions and (2) with intent to achieve optimal balloon to tissue contact the operator was biased to choosing a smaller balloon size, resulting in higher conformability (softer balloon).

Unlike in previous studies, the differences in IASA were driven by the larger IASA-R. The anatomical relation of transseptal access to the right PV ostia may explain this. The longitudinal RSPV axis is directed anterior-superior. By pushing the balloon to the RSPV ostium the more proximal CB parts are pushed against the posterior LA wall, creating a broad zone of contact. This is well in line with the results of remapping studies following an index CB-guided PVI, demonstrating that most LA-to-PV reconstructions occur at the opposite anterior right PV ostium.

In contrast, at the lateral PVs the CB is well aligned with the PV axis.

Clinical Implications
Early studies on the use of the big CB have already indicated the feasibility of antral PVI by reporting the “cross-talk” phenomenon. For the LB a circumferential PVI strategy may be achieved in a subset of lateral but not septal PVs and has been demonstrated to be inferior to a sequential approach. In patients with PAF the durability

![Figure 5](image-url)
of electrical PVI may outweigh the incremental value of more proximal lesions. This explains the remarkable success rates of LB in comparison with CB.26 Moreover, remapping studies after RF-guided procedures report disappointing results, while LB-treated patients display high chronic isolation rates even outperforming the 1st-generation CB.14,16,26,27

In the present analysis, CB-guided ablation gave the largest ISA. However, neither IASA nor ISA was identified as a predictor of clinical success. In this context, it needs to be pointed out that the study was not powered to investigate differences in clinical outcome and that the results may have been confounded by non-homogeneous patient groupings (30% and 10% patients with persistent AF in the LB and CB groups, respectively). Ultimately, only large prospective randomized trials with adequate statistical power will be able to compare clinical outcome between technologies.

In persistent AF a considerable fraction of patients remain free of recurrence after pure PVI (so-called PV responders).28,29 In others elimination of extra PV triggers, ganglionicated plexi and rotors is desirable. Because many ganglionicated plexi and rotors are located in close proximity to the antral PV region large IASAs would be preferable in the treatment of persistent AF. The present data and a recent clinical study suggest the feasibility of using the 28-mm CB even in patients with persistent AF.26 The true value of balloons in this patient population, however, deserves further investigation.

Study Limitations

The sample size of our population was quite small and the study was not powered to investigate differences in clinical outcome. Finally, the results may have been confounded by the non-homogeneous patient grouping (30% and 10% patients with persistent AF in the LB and CB groups, respectively).

Conclusion

Balloon-guided PVI was associated with antral lesion formation. CB-guided PVI was associated with the largest ISA as compared with LB procedures. ISA size did not correlate with clinical outcome after a single procedure in the present study population.

Funding

The study was supported by a research grant of CardioFocus™.

Conflicts of Interest

L.P. received a grant from the European Heart Rhythm Association. B.S., S.B. and K.R.J.C. have received speakers’ honoraria from CardioFocus™; A.F. and K.R.J.C. from Medtronic.

References


