Ablation Index for Catheter Ablation of Atrial Fibrillation — Clinical Applicability and Comparison With Force-Time Integral —

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Background: Key determinants for lesion formation in catheter ablation are contact force, radiofrequency (RF) power and time. The aim of this study was to evaluate the clinical applicability of ablation index (AI), a novel non-linear formula based on these components, and to compare AI with the conventional linear force-time interval (FTI) in pulmonary vein isolation (PVI).

Methods and Results: Target AI ranges were defined for anatomical segments of the ipsilateral pulmonary veins. The operator was blinded to AI during PVI for the initial 11 patients (group A), and was unblinded for the remaining 23 patients (group B). We assessed (1) the clinical value of AI to avoid excessively high and low values with an operator blinded vs. non-blinded to AI; and (2) the relation of AI and FTI in predefined ranges. In group A, 235/564 lesions (41.7%) were in the predefined target range as compared with 1171/1,412 lesions (82.9%) in group B (P<0.001). A given AI may correspond to a wide range of FTI, as reflected by a quartile coefficient of dispersion for AI of 0.11 vs. a quartile coefficient of dispersion for FTI of 0.36.

Conclusions: Incorporating RF current power, the non-linear AI provides more comprehensive information during PVI compared with FTI. Given that the FTI for a given AI varies widely, the value of FTI in clinical practice is questionable.

Key Words: Atrial fibrillation; Catheter ablation; Contact force; Lesion formation; Pulmonary vein isolation

Precise lesion formation is crucial for successful catheter ablation of atrial fibrillation (AF). Key determinants for lesion formation using radiofrequency (RF) ablation are contact force (CF), time and RF power. Insufficient RF delivery may result in ineffective lesion formation, whereas excessive RF current (RFC) delivery may result in potentially life-threatening complications such as atrio-esophageal fistula formation or cardiac tamponade. Reliable and clinically applicable feedback parameters are essential for ablation monitoring and to adequately regulate RF delivery to avoid complications and to keep AF recurrence rates as low as possible.

CF and the force-time integral (FTI), the product of CF and ablation time, are the most widely used parameters to control RFC applications. Low CF and FTI during AF ablation are associated with a higher incidence of pulmonary vein (PV) reconnection and recurrence of atrial arrhythmia. But even after initially successful PV isolation (PVI), the incidence of reconnection due to gaps in ablation lines is still high.

CF sensing catheters are now routinely adopted for catheter ablation of cardiac arrhythmias, but FTI has several limitations. First, it does not take into account RF power. The effect of increased power has been shown to be more significant compared with increased CF. Second, FTI assumes a linear relationship between CF and time. In recent studies, however, the ablation depth graphs reflected a non-linear relationship with time for diverse CF and RF power settings. The novel ablation index (AI; Biosense Webster, Diamond Barr, CA, USA) is intended to overcome these limitations. According to animal models, AI can precisely predict lesion size.

AI is a commercially available parameter that combines CF, RF time and RF power in a non-linear formula in real time. It therefore allows for intra-procedural visualization of RFC application in a 3-D electroanatomic mapping...
system (Carto 3, Biosense Webster). Recent adoption of AI in clinical practice has produced a significant improvement in procedural outcome\(^8\) and reduced 1-year recurrence rates.\(^3\) In initial clinical studies low AI has been associated with acute and late PV reconnection.\(^11,12\) AI-guided PVI is associated with higher impedance drop and AI is used as a surrogate parameter for effectiveness of lesion formation.\(^13,14\) AI, however, is not yet widely used in clinical practice. Recently, we have adopted the intra-procedural use of the parameter as an institutional standard for RFC treatment of symptomatic paroxysmal AF was performed in power-controlled mode. RFC application was limited to 35 W at the anterior and to 25 W at the roof and posterior segment, respectively, to take into account differing thickness of the myocardial wall and to avoid potential complications such as steam pop formation or esophageal injury. Target AI was 380 for the posterior segment, 450 for the roof segment and 500 for the anterior segment. Importantly, no dragging technique was used. RFC energy was delivered with a target CF of 10–40 g until a signal reduction of 70% was achieved. Applications <5 s were excluded from analysis. All procedures were performed by 1 single operator.

**Methods**

**Patients**

The subjects consisted of 34 patients diagnosed with symptomatic paroxysmal AF defined as >1 episode of AF <7 days duration with ≥1 episode documented on 12-lead electrocardiogram.\(^15\) Patients with prior left atrial (LA) catheter ablation were excluded. Data were obtained from the institutional ablation registry and analyzed retrospectively. Written informed consent was obtained from all patients. The study was approved by the institutional ethics committee. All patients underwent PVI for paroxysmal AF according to the institutional standard.

**PVI**

To exclude LA thrombus, all patients underwent transesophageal echocardiography 1 day prior to the procedure. Intake of novel oral anticoagulation was discontinued 24 h before the procedure. Oral anticoagulation with phenprocoumon was continued and the international normalized ratio was maintained at 2.0–3.0. All patients underwent PVI in deep sedation applying a continuous i.v. infusion of propofol with additional boluses of midazolam and fentanyl. As per the institutional standard, no esophageal temperature monitoring was performed.

A decapolar catheter was advanced into the coronary sinus. After double trans-septal puncture, 2 SL1 sheaths were advanced into the LA. A commercially available navigated decapolar spiral mapping catheter (LASSO, Biosense Webster) was used for PV mapping. A 3-D electroanatomic map of the LA was obtained using either a point-by-point technique with a CF-sensing catheter (ThermoCool SmartTouch Surround Flow [STSF], Biosense Webster) or a fast anatomic mapping technique using the spiral catheter. Anatomical segments of the PV were arbitrarily defined as anterior, roof and posterior segments of the ipsilateral PV. Wide area circumferential PVI was performed in deep sedation applying a continuous i.v. infusion of propofol with additional boluses of midazolam and fentanyl.

**Table. Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.7±11.5</td>
</tr>
<tr>
<td>Male</td>
<td>64.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.3±5.5</td>
</tr>
<tr>
<td>CHA2DS2-Vasc score (no. patients)</td>
<td>1.3±1.4</td>
</tr>
<tr>
<td>&lt;2</td>
<td>13</td>
</tr>
<tr>
<td>2–4</td>
<td>6</td>
</tr>
<tr>
<td>&gt;4</td>
<td>4</td>
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<tr>
<td>Hypertension</td>
<td>76.5</td>
</tr>
<tr>
<td>CAD</td>
<td>32.3</td>
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<tr>
<td>Diabetes mellitus</td>
<td>17.6</td>
</tr>
<tr>
<td>COPD</td>
<td>5.9</td>
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<tr>
<td>LVEF (%)</td>
<td>54.5±3.5</td>
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<tr>
<td>LAD (mm)</td>
<td>37.5±3.8</td>
</tr>
<tr>
<td>Medication</td>
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<tr>
<td>β-adrenergic blocker</td>
<td>85.3</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>26.5</td>
</tr>
<tr>
<td>ACEI</td>
<td>29.4</td>
</tr>
<tr>
<td>Calcium-channel blocker</td>
<td>32.3</td>
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<tr>
<td>Sodium-channel blocker</td>
<td>44.1</td>
</tr>
<tr>
<td>Oral anticoagulant</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Data given as % or mean±SD, unless otherwise indicated. ACEI, angiotensin-converting enzyme inhibitor; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; LAD, left atrial diameter; LVEF, left ventricular ejection fraction.
Ablation Index for PVI

were enrolled in the study. Patient characteristics are listed in Table.

Procedural Data and Outcome
PVI was successfully achieved in all patients and no major periprocedural complication occurred. Mean procedure duration was 144±38 min. Mean dose-area product was 3,070.6±2,034.6 cGy·cm² and mean radiation duration was 15.5±6.2 min. Median procedure time did not differ between groups: group A, 144 min (IQR, 40 min); group B, 143 min (IQR, 46.5 min; P=0.70). There was no difference in total ablation time, maximum contact force, maximum temperature, baseline impedance or impedance drop between blinded and non-blinded AI (Figure 1). After a mean follow-up of 639.0±92.9 days, with 1 patient lost to follow-up in group B, the number of recurrences was 4/11 in group A and 7/22 in group B (P=1.0, Fisher's exact test). There were no complications in group A, as opposed to 2 complications in group B (1 post-procedural transitory ischemic attack, 1 groin hematoma not requiring surgical therapy; P=0.54, Fisher’s exact test).

Blinded vs. Non-Blinded
A total of 1,967 ablation points (group A, 564 points, 28.5%; group B, 1,412 points, 71.5%) were included in the analysis. For group A, median AI at the anterior, the posterior and the roof segment was 457 (IQR, 175–707); 426 (IQR, 175–670) and 469 (IQR, 160–787), respectively, for the left PV and 498 (IQR, 166–833); 425 (IQR, 107–722) and 490 (IQR, 237–731), respectively, for the right PV. Median AI in group B (non-blinded) at the anterior, the posterior and the roof segment was 461 (IQR, 261–665); 465 (IQR, 231–725) and 442 (IQR, 439–474), respectively for the left PV

Statistical Analysis
Statistical analysis was performed with R (R: A Language and Environment for Statistical Computing, R Core Team, R Foundation for Statistical Computing, Vienna, Austria, 2017. https://www.R-project.org). Data sets from both patient groups were filtered for a minimal duration of 5s. Non-normally distributed continuous variables are represented as median (IQR). Kolmogorov-Smirnov test was used to test for normality of distributions. To assess the proportion of values in a target range as a categorical variable, Fisher’s exact test was used. Statistical significance was set at P<0.05. To estimate dispersion of non-normally distributed data, the quartile coefficient of dispersion was applied. Pearson correlation coefficient was used for correlation analyses of AI and FTI.

Results
Thirty-four patients with symptomatic paroxysmal AF were enrolled in the study. Patient characteristics are listed in Table.

Procedural Data and Outcome
PVI was successfully achieved in all patients and no major periprocedural complication occurred. Mean procedure duration was 144±38 min. Mean dose-area product was 3,070.6±2,034.6 cGy·cm² and mean radiation duration was 15.5±6.2 min. Median procedure time did not differ between groups: group A, 144 min (IQR, 40 min); group B, 143 min (IQR, 46.5 min; P=0.70). There was no difference in total ablation time, maximum contact force, maximum temperature, baseline impedance or impedance drop between blinded and non-blinded AI (Figure 1). After a mean follow-up of 639.0±92.9 days, with 1 patient lost to follow-up in group B, the number of recurrences was 4/11 in group A and 7/22 in group B (P=1.0, Fisher’s exact test). There were no complications in group A, as opposed to 2 complications in group B (1 post-procedural transitory ischemic attack, 1 groin hematoma not requiring surgical therapy; P=0.54, Fisher’s exact test).

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Figure 1. Ablation parameters for procedures where the operator was blinded vs. non-blinded to ablation index (AI) during the procedure. There was no difference between groups for procedural (A) total ablation time [min], (C) maximum contact force [g], (D) maximum temperature [°C], (E) maximum power [W], (F) baseline impedance [Ω] or (G) impedance drop [Ω]. (B) Ablation time per lesion [s], however, was significantly shorter when AI was displayed.
There was no difference in AI between group A and group B (P=0.631, Wilcoxon test). Median ablation parameters did not differ between groups with respect to ablation time (24.2 min vs. 24.2 min), maximum contact force (19.9 g vs. 18.4 g), maximum temperature (26.9°C vs. 26.9°C), maximum power (25.8 W vs. 25.9 W), baseline impedance (154.0 Ω vs. 154.8 Ω) or impedance drop (7.3 Ω vs. 8.2 Ω).

Display of AI (group B) resulted in a significantly higher rate of ablation points in the predefined target range as compared with blinded ablation: group A, 235/564 (41.7%) vs. group B, 1,171/1,412 (82.9%; P<0.001), so that very low or very high AI outside the target range were avoided.

Figure 2. Proportion of ablation points in the ablation index (AI) target range (±15% of target values, i.e. 500, 380 and 450 for anterior, posterior and roof segment, respectively) when the operator was (Left) blinded or (Right) non-blinded to AI during the procedure.

Figure 3. Relation between force-time integral (FTI) and ablation index (AI) when the operator was (A) blinded or (B) non-blinded to AI during the procedure. (B) When AI was displayed, ablation was performed to AI target values of 500 for anterior, 380 for posterior, and 450 for roof segments, resulting in (C, Lower) distinct peaks of AI in the respective segments. (C, Upper) Corresponding FTI does not exhibit distinct peaks, but is widely distributed. (D) Consequently, corresponding FTI for grouped AI has a wider range.

and 510 (IQR, 479–547); 381 (IQR, 358–422) and 452 (IQR, 435–481), respectively, for the right PV.
Median ablation time per lesion was longer in group A (24.5 s) versus group B (22.0 s; Figure 1). AI below the target range was registered for 90 points (16%), 25 points (4.4%) and 32 points (5.7%) for the anterior, roof and posterior segment, respectively, in group A, and for 97 points (6.9%), 46 points (3.3%) and 35 points (2.5%) for the anterior, roof and posterior segment, respectively, in group B. AI above the target range was registered for 49 points (8.7%), 44 points (7.8%) and 89 points (15.8%) for the anterior, roof and posterior segment, respectively, in group A and for 18 points (1.3%), 16 points (1.1%) and 29 points (2.0%) for the anterior, roof and posterior segment, respectively in group B (Figure 2).

AI vs. FTI
For very low AI (0–300 AU) FTI ranged from 174 to 512 s; for low AI (300–400 AU) FTI ranged from 331 to 572 s; for high AI (400–500 AU), from 357 to 604 s; for very high AI (500–600 AU) from 215 to 1,220 s; and for excessively high AI (>600 AU), FTI ranged from 477 to 4,369 s. AI and FTI did correlate (R=0.70); distinct AI may exhibit a wide range of corresponding FTI (Figure 3). For 74/1,976 points (3.7%) FTI was >400 and AI was below the target range of the respective segment.

Generally, FTI varies more widely compared with AI, which is reflected by the quartile coefficient of dispersion, for which AI was 0.11 and 0.36 for FTI.

FTI increases linearly whereas AI is characterized by a non-linear growth reflective of lesion formation.16 Figure 4 shows representative lesions and the increase of FTI and AI over time, illustrating the wide range of FTI for a given AI.

Discussion
In this study we have demonstrated that AI is a clinically applicable tool that allows for more standardized RFC applications. When compared with the established parameter, the dispersion of FTI is larger, whereas RFC application can easily be adjusted to a narrow range of AI. As demonstrated by Figure 4, FTI increases linearly whereas AI is characterized by a non-linear growth, reflective of lesion formation. Especially for high AI, FTI can vary widely. For CF as a feedback parameter, display of CF resulted in greater stability of the CF values.17 A higher proportion of AI values were in the target range when AI was displayed to the operator. The ablation parameters ablation time, maximum CF, maximum temperature, maximum power, baseline impedance and impedance drop did not differ between group A and group B, although ablation time per lesion was shorter in group B. Shorter ablation time per lesion may be explained by a more rigorous point-by-point ablation technique. Outcome and complication rates did not differ between the groups, but the sample size was a limited, and hence the study was not sufficiently powered for an assessment of recurrence rates and incidence of complications. A major shortcoming of CF is its high variability related to anatomical and respiration-caused instability, also when visible to the operator.7,18 In contrast to the corresponding AI ranges, FTI has a large proportion of overlapping values: FTI considered acceptable may correspond to AI in the target range but also to AI below the accepted target range. This demonstrates that FTI may be misleading, notably because high CF can correspond to small lesions.19 Therefore, when compared with FTI, as an established parameter to control RFC application, AI is more stable and reliable. Similarly to the current findings, impedance drop is a poor predictor of adequate RFC delivery due to its large variability.17 Additionally, for high AI – around 500 as recommended for the anterior wall of the LA – FTI has a wide dispersion, thereby limiting the clinical applicability of FTI.

The principal shortcoming of FTI is its linearity, which does not correspond to the mechanism of lesion formation, which is best approximated in a non-linear formula, incorporating power.1 These requirements are met by AI, with the respective target values according to the anatomical segment.11,20

Prevention of low AI has the potential to improve efficacy, whereas avoiding high AI may improve safety. Integration of AI into clinical routine may be useful to achieve more homogeneous lesion formation and allow for more standardized ablation procedures.

We therefore suggest the adoption of AI as a real-time feedback parameter as a clinical standard.

Study Limitations
The present evaluation is a retrospective and observational
non-randomized study with a limited number of patients. Randomized studies with a larger sample size would be necessary to assess PVI outcome when adopting AI as a procedural feedback tool. In the present study, an assessment of conduction gaps during waiting time or of dormant conduction after PVI was not performed.

Conclusions

When displayed to the operator, a larger proportion of ablation points are located in the defined target range, thereby avoiding low AI, potentially resulting in ineffective ablation, as well as excessively high AI, potentially resulting in complications such as steam pop formation, cardiac perforation or collateral damages such as atrio-esophageal fistula formation.

Given that the non-linear AI incorporates RFC power, it provides more information on lesion formation during perforation or collateral damages such as atrio-esophageal fistula formation.

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Disclosures

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