Impact of Box Isolation on Rotors and Multiple Wavelets in Persistent Atrial Fibrillation

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Background: Additional benefits of posterior left atrial (LA) box isolation (BOXI) over pulmonary vein isolation (PVI) in persistent atrial fibrillation (perAF) have been reported, but the mechanism is still unclear. We evaluated the effects of BOXI on rotors and multiple wavelets in the whole LA.

Methods and Results: Twenty patients with perAF (including 12 cases of longstanding perAF) underwent PVI. Real-time phase mapping (ExTra Mapping) was performed in the whole LA during AF. Subsequently, BOXI was added and re-ExTra Mapping was performed again at the same site. The nonpassively activated ratio (%NP), the ratio of the form of rotors and multiple wavelets to the recording time, was compared before and after BOXI. After BOXI, the %NP significantly decreased in the anterior wall (from 53±22% to 39±23%, P=0.010), inferior wall (from 51±16% to 34±19%, P=0.001), and LA appendage (from 23±27% to 16±19%, P=0.049). However, there were no significant differences in the septum (49±19% vs. 49±18%, P=0.562) or lateral wall (41±19% vs. 38±15%, P=0.526).

Conclusions: BOXI not only reduced the critical mass for maintenance of AF, but also decreased the rotors and multiple wavelets in the anterior wall, inferior wall and LA appendage during perAF.

Key Words: Atrial fibrillation; Box isolation; Catheter ablation; Phase mapping; Pulmonary vein isolation

Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation of atrial fibrillation (AF) and highly effective in paroxysmal AF. However, it may not be enough to cure persistent or longstanding AF, and further modification of the atrial substrate may be necessary. Previous studies have demonstrated that the posterior left atrium (LA) plays an important role as the AF substrate, including conduction delay, triggers and drivers. Addition of the posterior LA Box isolation (BOXI) over PVI in persistent AF (perAF) have been reported in previous studies.

On the other hand, an individualized approach to AF ablation based on low-voltage areas (LVAs), which correlate with atrial fibrosis, has been proposed. However, we demonstrated that additional ablation of LVAs after BOXI did not significantly improve the success rate in perAF patients with LVAs. It is unclear why the LVAs outside of the posterior LA were not related to the outcomes. Therefore, we evaluated the effects of BOXI on rotors and multiple wavelets in the whole LA using a novel real-time phase mapping system.

Methods

Patients’ Characteristics

The study group comprised 25 consecutive patients with perAF (n=11) and longstanding perAF (n=14) underwent catheter ablation. AF was terminated in 1 patient during PVI and in 4 patients during BOXI, so these 5 patients were excluded from the study. The study population therefore consisted of 20 patients with perAF (n=8) and longstanding perAF (n=12). Their clinical characteristics are shown in Table 1. All patients were taking a direct oral anticoagulant before the ablation. Transesophageal echocardiography was performed on the day before the procedure in all patients. All antiarrhythmic drugs were stopped at least 5 half-lives before the procedure. Amiodarone was not prescribed in any patients.

PerAF was defined as AF that was sustained for >7 days but which required pharmacologic or electrical cardioversion. Longstanding perAF was defined as continuous AF that had lasted >1 year. Written informed consent was given by all patients and the study was approved by the Fukuoka Sanno Hospital’s Institutional Review Board.

Preparation

A duo-decapolar catheter (Bee-AT, Japan-Lifeline Co., Ltd., Tokyo, Japan) was inserted in the coronary sinus from the right internal jugular vein. After a double transseptal puncture, a 20-pole circular mapping catheter (Optima™ or Reflexion HD™, St. Jude Medical, St. Paul, MN, USA) and irrigated-tip ablation catheter (FlexAbility™, St. Jude

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AF, atrial fibrillation; BNP, B-type natriuretic peptide; LA, left atrium; LVEF, left ventricular ejection fraction.

**Table 1. Patients' Characteristics**

| Characteristic                  | Mean ± SD |
|---------------------------------|-----------|
| Age, years                      | 61 ± 9    |
| Female, n (%)                   | 2 (10)    |
| Duration of AF, months          | 29 ± 26   |
| Longstanding persistent AF, n (%)| 12 (60)  |
| CHADS2 score                    | 0.7 ± 1.0 |
| BNP, pg/mL                      | 98 ± 61   |
| LA diameter, mm                 | 46 ± 6    |
| LVEF, %                         | 62 ± 7    |
| LA appendage flow, cm/s         | 35 ± 15   |

**Results**

PVI was completely achieved in all patients, after which the ExTrA Mapping was performed and sufficient contact of all electrodes could be obtained in all areas in all patients.

**Analysis of Consecutive Activation Patterns of the Posterior LA During AF**

Figure 1 presents the electrograms and consecutive activation maps of ExTrA Mapping of the posterior LA during AF after PVI. The mean AF cycle length was 167 ms (Figure 1A). In Figure 1B, window 1 (top) shows that a wave front traveling from the LA roof merged with a wave coming from the inferior wall (window 1, bottom) and formed a rotor lasting for 3 rotations (windows 1–8) with a cycle length of 170 ms. In window 10 (bottom), a wave front traveling from the inferior wall moved away to the roof. In this case, the %NP was 54%. Thus, in this case, multiple wavelets traveling from the LA roof and septum merged and formed a rotor, but reentry was unstable and short-lived. Wave fronts traveling from the anterior LA and the inferior wall may play an important role in the formation of rotors.

**BOXI**

BOXI was completely achieved in all patients (Figure 2A), after which the entrance block of the Box lesion was confirmed by complete electrical silence in the posterior LA (Figure 2B).
Impact of BOXI on Rotors

Figure 1. (A) Electrograms of the posterior left atrium (LA) before BOXI. Intraatrial bipolar electrograms recorded by a 20-pole spiral-shaped catheter during atrial fibrillation (AF) are shown. Mean AF cycle length is 167 ms. (B) ExTRa Mapping of the posterior LA before BOXI. The activation sequences during 720 ms of data (60 ms x 12 consecutive time windows) are shown. White lines indicate the head of the wave fronts, and white arrows indicate the direction of the wave fronts. In this case, a wave front traveling from the LA roof forms a rotor lasting for 3 rotations. The nonpassively activated ratio (%NP) is 54%. BOXI, Box isolation.
fronts traveling from the posterior LA may play an important role in the formation of rotors. Figure 4 presents the ExTRA Mapping of the anterior LA during the same AF episode as shown in Figure 3 after BOXI. The mean AF cycle length was 178 ms (Figure 4A). In Figure 4B, a wave front coming from the lateral wall (window 1, right) merged with a new wave from the LA roof (window 9, right) and formed a rotor lasting for 1 rotation. In this case, the %NP was 32%. Thus, after BOXI, wave fronts traveling from the posterior LA across the LA roof were not observed, only those traveling from the septum and lateral wall. These wave fronts disappeared,
Figure 3.  (A) Electrograms of the anterior left atrium (LA) before BOXI. Mean AF cycle length is 157 ms. (B) ExTRa Mapping of the anterior LA before BOXI. In this case, 2 wave fronts traveling from the LA roof and lateral wall formed a rotor lasting for 2.5 rotations. A wave front coming from the lateral wall (window 9) merged with a new wave from the LA roof (window 10) and formed a rotor lasting for 1 rotation. The nonpassively activated ratio (%NP) is 75%. BOXI, Box isolation.
Figure 4.  (A) Electrograms of the anterior left atrium (LA) after BOXI. This is the same AF episode as shown in Figure 3. Mean AF cycle length is 178 ms.  (B) ExTRa Mapping of the anterior LA after BOXI. After BOXI, the wave fronts traveling across the LA roof from the posterior LA are not observed, only those traveling from the septum and lateral wall. These wave fronts disappear, and no rotors are observed. The nonpassively activated ratio (%NP) is 32%. BOXI, Box isolation.
and no rotor formed.

Similar activation patterns were observed in other cases, although with minor differences.

Comparison of %NP Before and After BOXI

Table 2 shows a comparison of the %NP before and after BOXI. After BOXI, it significantly decreased in the anterior wall (from 53±22% to 39±23%, P=0.010), inferior wall (from 51±16% to 34±19%, P=0.001), and LAA (from 23±27% to 16±19%, P=0.049). However, there were no significant differences in the septum (49±19% vs. 49±18%, P=0.562) or lateral wall (41±19% vs. 38±15%, P=0.526).

Clinical Outcomes

After a single procedure, 16 (80%) of 20 patients had no recurrence of atrial tachyarrhythmia during 12±4 months of follow-up.

Discussion

Main Findings

The present study demonstrated that (1) rotors and multiple wavelets were still observed in the whole LA even after PVI in patients with perAF, (2) wave fronts traveling to and from the anterior or posterior wall may play an important role in the formation of rotors, and (3) BOXI can not only eliminate the rotors and multiple wavelets within the posterior LA, but also decrease them in the anterior wall, inferior wall and LAA.

ExTRa Mapping in perAF

Sakata et al23 demonstrated that real AF drivers were contained in the nonpassively activated areas where rotors and/or multiple wavelets were most frequently observed during the 5-s recording time, which was decided according to reproducibility. Although the recording time seems short, the reproducibility of the %NP was high.23

In the present study using ExTRa Mapping, multiple wavelets merged, the wave front shape was highly curved and formed rotors, but the rotor was unstable and short-lived. Wave fronts traveling to and from the anterior or posterior wall may play an important role in the formation of rotors.

Mechanism of the Beneficial Effects of BOXI in perAF

Previous studies have shown that BOXI in addition to PVI results in a better outcome than PVI alone or PVI plus roofline ablation in patients with perAF.10–18 It is possible that BOXI can eliminate the triggers and rotors in the posterior LA. We have demonstrated that BOXI facilitated AF termination and its non-inducibility.11 Moreover, BOXI can serve as LVA ablation when LVAs are localized to the posterior LA. However, we have shown that addition of LVA ablation to BOXI did not significantly improve the success rate in perAF patients with LVAs.11 It was unclear why the LVAs on the anterior wall were not related to the outcomes. As shown in Figure 4, after BOXI, the wave fronts traveling from the posterior LA were blocked and no rotors were observed on the anterior wall. BOXI may prevent fibrillatory conduction of wave fronts emanating from rotors within the posterior wall, at the same time reducing the overall frequency of activation. Therefore, BOXI may decrease the rotors and multiple wavelets in the anterior wall, inferior wall and LAA. However, there were no changes in the septum and lateral wall, which may be because of the wave fronts traveling from the right atrium and coronary sinus. Those results may explain why BOXI resulted in a better outcome than PVI alone or PVI plus roofline ablation, and why LVA ablation showed no benefit over BOXI in patients with perAF. Moreover, a previous study using the ExTRa Mapping system has shown that not all rotors were included in LVAs.23

Study Limitations

We did not perform RF ablation at rotor sites, so it remains unclear whether transient rotors were critical to AF maintenance. However, Sakata et al23 demonstrated that ExTRa Mapping-guided ablation of areas with a high %NP had a potential benefit beyond PVI.

Conclusions

BOXI can not only reduce the critical mass for maintenance of AF within the posterior LA, but also decrease the rotors and multiple wavelets in the anterior wall, inferior wall and LAA during perAF.

Conflict of Interest

The authors have received remuneration from the Nihon Kohden Corporation.

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