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Atrioventricular conduction disturbance during pulmonary vein isolation using the second-generation cryoballoon — Vagal impact of cryoballoon ablation

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ABSTRACT

Background: Vagal reactions of the sinus node during pulmonary vein isolation (PVI) have been reported, however, data on intra-procedural atrioventricular conduction disturbances have been sparse. The present study aimed to investigate the clinical characteristics of atrioventricular conduction block (AVB) during PVI using second-generation cryoballoons.

Methods: A total of 2252 PVs among 568 consecutive atrial fibrillation patients undergoing PVI with 28-mm cryoballoons were analyzed. In 44 patients, left superior PVs (LSPVs) were initially targeted (initial-LSPV-group). In the remaining 524 patients, LSPVs were targeted following right superior PVs (RSPVs) (initial-RSPV-group).

Results: Marked sinus arrests/bradycardia occurred in 14 patients only in the initial-LSPV-group, and the incidence was significantly higher in the initial-LSPV than initial-RSPV-group (14/44 vs. 0/524, $p < 0.001$). Intra-procedural AVB with 3.6 [1.9–8.2] second maximal RR intervals appeared in 12 patients during freezing ($n = 1$) or after balloon deflation following freezing ($n = 11$). The targeted PVs were the LSPV, left common PV, right inferior PV, and RSPV in 8, 1, 2, and 1 patients, respectively. The incidence was similar between the initial-LSPV and initial-RSPV-groups (1/44 vs. 11/524, $p = 0.938$). Four patients exhibited complete AVB with more than a 6 s maximal RR interval. Three patients experienced AVB during atrial fibrillation. AVB was observed a median of 23.0 [15.0–70.0] seconds after balloon deflation and 76.0 [60.0–125.0] seconds after freezing termination. AVB persisted for 56.0 [36.0–110.0] seconds, and all recovered spontaneously with or without requiring back-up pacing.

Conclusions: A marked transient AV conduction disturbance could occur after balloon deflation, especially during LSPV ablation, regardless of the order of targeted PVs.

1. Introduction

Pulmonary vein isolation (PVI) has been established in radiofrequency catheter ablation of atrial fibrillation (AF) [1,2]. The cryoballoon is an alternative tool for PVI, and has a comparable efficacy and safety to radiofrequency ablation [3,4]. The recently introduced second-generation CB has provided a higher performance and has allowed for shorter application and procedure times than the predecessor [5–7].

It is well known that PVI can have an impact on the cardiac autonomic nervous system via the ganglionated plexi (GP) located at the PV antrum, regardless of the energy source [8–11]. Sinus arrest could occur during ablation of the left PVs, and the heart rate could increase during ablation of the right superior PV [8–11]. These reactions of the sinus node during the PVI have been reported, however, reports on the impact of the PVI on the atrioventricular (AV) conduction have been sparse. Generally, AV conduction disturbances are not observed during the PVI with radiofrequency ablation. However, it might be possible that the PVI has an influence on the AV conduction with second-generation CB ablation, given the different mechanisms of the lesion creation and greater extent of myocardial injury as compared to radiofrequency ablation [12]. The present study aimed to investigate the incidence and clinical characteristics of AV conduction disturbances during PVI using second-generation CBs.

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2. Methods

2.1. Study population

This study consisted of 568 consecutive patients with AF who underwent an index PVI using a second-generation CB (Arctic Front Advance, Medtronic, Minneapolis, MN) in our institute. The PVI was performed with a single balloon technique using a 28-mm CB. In 44 (7.7%) patients, the PVI was performed starting with the left (left superior [LS] and then left inferior [LI] PV) and then followed by the right PVs (right superior [RS] and then right inferior [RI] PV) (initial-LSPV group). In the remaining 524 (92.3%) patients, the left PVs were targeted after the right PVs (initial-RSPV group). AF was classified according to the latest guidelines [2]. All patients gave their written informed consent. The study protocol was approved by the hospital's institutional review board. The study complied with the Declaration of Helsinki.

2.2. Mapping and ablation protocol

All antiarrhythmic drugs were discontinued for at least five half-lives prior to the procedure. Pre-procedural cardiac enhanced computed tomography was performed to evaluate the cardiac anatomy. The surface electrocardiogram and bipolar intracardiac electrograms were continuously monitored and stored on a computer-based digital recording system (LabSystem PRO, Bard Electrophysiology, Lowell, MA). The bipolar electrograms were filtered from 30 to 500 Hz. The procedure was performed under dexmedetomidine-induced moderate sedation. A 100 IU/kg heparin bolus was administered immediately following the venous access, and heparinized saline was additionally infused to maintain the activated clotting time at 300–350 s. A single transseptal puncture was performed using a radiofrequency needle (Baylis Medical, Inc., Montreal, QC) and 8-Fr long sheath (SL0, AF Division, SJM, Minneapolis, MN). The transseptal sheath was exchanged over a guidewire for a 15-Fr steerable sheath. A 20-mm circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA) was used for mapping the PVs before and after the cryoablation to confirm the PVI. A spiral mapping catheter (Achieve, Medtronic) was used to map the PV potentials. Complete sealing at the PV antra with a 28-mm CB was confirmed by a contrast medium injection. No 23-mm CBs were used in any cases. This was followed by a freeze cycle of 180 s without a bonus application after the isolation. In order to avoid any phrenic nerve injury [13], the CB applications were applied under diaphragmatic electromyography monitoring. Additional touch-up ablation was performed if deemed necessary.

2.3. Definition of autonomic responses

An intra-procedural vagal reaction was defined as sinus bradycardia (<40 bpm), asystole, AV block, or hypotension that occurred during the balloon inflation, manipulation, freezing, thawing, deflation, or after the deflation, according to the previously reported definition [8–11]. Temporary pacing was performed when the cycle length prolonged during the procedure.

2.4. Statistical analysis

Continuous data are expressed as the mean ± standard deviation for normally distributed variables or as the median [25th, 75th percentiles] for non-normally distributed variables, and were compared using a Student's *t*-test or Mann-Whitney *U* test, respectively. Categorical variables were compared using the chi-square test. A probability value of $p < 0.05$ indicated statistical significance.

3. Results

3.1. Clinical characteristics and procedure results

A total of 568 consecutive patients (475 paroxysmal, and 93 non-paroxysmal AF) who underwent an index second-generation CB ablation were included, and a total of 2252 PVs were analyzed. Overall, 2172 of 2252 (96.5%) PVs were isolated successfully using exclusively a 28-mm second-generation CB. The total number of CB applications was 5.0 ± 1.4 per patient, and the mean number of CB applications was 1.2 ± 0.6, 1.2 ± 0.5, 2.9 ± 1.3, 1.2 ± 0.4, and 1.4 ± 0.8 for the LSPV, LIPV, left common PV (LCPV), RSPV, and RIPV, respectively. The nadir balloon temperature was −50.8 ± 5.1, −45.5 ± 5.1, −54.7 ± 5.1, and − 51.9 ± 6.4 °C in the LSPV, LIPV, RSPV, and RIPV, respectively. Touch-up lesions were created in the remaining 80 (3.5%) PVs including 10, 15, 1, 7, and 47 in the LSPV, LIPV, left common PV, RSPV, and RIPV, respectively. In total, all 2252 PVs were successfully isolated by catheter ablation.

3.2. Intra-procedural vagal reactions

Intra-procedural sinus arrest/bradycardia occurred in 14 patients all in the initial-LSPV group, and none in the initial-RSPV group. A marked sinus bradycardia/arrest was observed after the balloon deflation following freezing in all the cases. The incidence of an intra-procedural sinus bradycardia/arrest was significantly higher in the initial-LSPV group than initial-RSPV group (14/44 vs. 0/524, $p < 0.001$).

On the contrary, intra-procedural AV block appeared for a total of 13 events among 12 (2.1%) patients. One (8.3%) patient was in the initial-LSPV group and the remaining 11 (91.7%) were in the initial RSPV-group. The incidence of intra-procedural AV block was similar between the initial-LSPV group and initial-RSPV group (1/44 vs. 11/524, $p = 0.938$). The maximal RR interval during AV block was a median of 3.6 [1.9–8.2] seconds. Two and 3 patients experienced Wenckebach and 2:1 AV block, respectively, and the maximal RR interval was <3 s in this 5 (41.6%) patients. Four (33.3%) patients exhibited complete AV block, and the maximal RR interval was >6 s (Figs. 1–3). The remaining 3 (25.0%) patients experienced AV block during AF, and the maximal RR interval was between 3 and 6 s. One (8.3%) patient experienced 2:1 block during the freezing phase when targeting the RIPV, and it occurred 60 s after starting the freezing. The remaining 11 (91.7%) patients exhibited AV block after the balloon deflation following the freezing of the LSPV ($n = 8$), LCPV ($n = 1$), RSPV ($n = 1$), or RIPV ($n = 1$). One patient experienced complete AV block twice, reproducibly following an LCPV ablation. AV block was observed at a median of 23.0 [15.0–70.0] seconds after the balloon deflation and 76.0 [60.0–125.0] seconds after the terminating the freezing. The AV block persisted for 56.0 [36.0–110.0] seconds, and all recovered spontaneously with or without requirement of back-up pacing. In all 12 patients, a PVI was successfully achieved with the CB. No patients experienced both sinus arrest and AV block, and no patients exhibited any other vagal responses.

3.3. Predictors of intra-procedural AV block

There was no significant difference in the baseline patient characteristics between the 12 patients with intra-procedural AV block and 556 patients without (Table 1). The diameter of the LSPV in the coronal (18.1 ± 0.9 vs. 17.2 ± 2.7 mm, $p = 0.548$) and horizontal views (13.8 ± 3.0 vs. 13.4 ± 2.6 mm, $p = 0.548$) of the cardiac CT (Fig. 3), and the nadir balloon temperature during the freezing (−50.6 ± 4.7 vs. −50.8 ± 5.1 °C, $p = 0.906$) did not significantly differ between the 8 patients with intra-procedural AV block during the LSPV ablation and 560 patients without. The nadir balloon temperature when subsequent AV block occurred was −54 and − 44 °C in the RSPV and RIPV in one patient each.

4. Discussion

The present study evaluated the intra-procedural vagal impact of CB ablation in a large study population. We found that: 1) preceding the RSPV ablation by an LSPV ablation could completely inhibit any intra-procedural sinus arrest/bradycardia, 2) the incidence of intra-procedural AV block was 2.1% (maximal RR interval >6 s in 0.7%) regardless of the order of the targeted PVs, 3) the timing of the occurrence was after balloon deflation following freezing in the vast majority of cases, and the timing was similar to the reported timing of intra-procedural sinus arrest/bradycardia occurrence, 4) it occurred after the LSPV ablation in the majority of the cases, but also could occur after the RSPV, RIPV, or LCPV ablation, 5) all recovered spontaneously with or without requirement of back-up pacing a few minutes later, and 6) there was no predictors of the occurrence.

4.1. Intra-procedural sinus arrest/bradycardia

The PVs and neighboring atrial tissue are richly innervated by the cardiac autonomic nervous system which consists of GPs [14]. The 5