International Journal of Cardiology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Does second-generation cryoballoon ablation using the current single short freeze strategy produce pulmonary vein stenosis?

Shinsuke Miyazaki *, Takatsugu Kajiyama [1], Masahiro Hada [1], Hiroaki Nakamura [1], Hitoshi Hachiya [1], Hiroshi Tada, Kenzo Hirao [2], Yoshito Iesaka [1]

Department of Cardiovascular medicine, Fukui University, Fukui, Japan

ARTICLE INFO

Article history:
Received 24 June 2018
Received in revised form 17 July 2018
Accepted 2 August 2018
Available online xxxx

Keywords:
Complication
Pulmonary vein stenosis
Cryoballoon
Catheter ablation
Atrial fibrillation

ABSTRACT

Background: Few data are available regarding pulmonary vein (PV) stenosis after second-generation cryoballoon PV isolation (CB2-PVI). Currently, a single short freeze strategy is standard for CB2-PVI owing to enhanced cooling effects. This study aimed to evaluate the incidence of PV stenosis after CB2-PVI with the current standard strategy.

Methods: Two hundred seventy-six atrial fibrillation patients underwent CB2-PVI using one 28-mm balloon and single 3-minute freeze strategy. If balloon temperatures reached −60 °C or phrenic nerve injury was suspected, freezing was terminated. Enhanced cardiac computed tomography (CT) was obtained before and >3 months after the procedure.

Results: Overall, 1067 of 1101 (96.9%) PVs were isolated with cryoballoons, while the remaining 34 PVs required touch-up ablation. The total application number/patient was 5.1 ± 1.4, and total application time 216 ± 104, 205 ± 77, 186 ± 68, and 246 ± 142 s for the left superior (LSPV), left inferior (LIPV), right superior (RSPV), and right inferior PVs, respectively. Follow-up CT obtained a median of 5.0 [3.3–7.0] months post-procedure revealed no PVs with moderate or severe stenosis. Asymptomatic mild stenosis was documented in 16 total (1.4%) PVs (5 LSPVs, 5 LIPVs, and 6 RSPVs), but not in right inferior, left common, right middle, or PVs requiring touch-up ablation. Mild stenosis did not progress during the follow-up. Among the potential factors associated with PV stenosis, longer application times were the sole significant factor associated with mild RSPV stenosis.

Conclusions: In CB2-PVI with the current single short freeze strategy, the risk of PV stenosis is extremely low, and routine follow-up imaging for evaluation seems not to be necessary.

1. Introduction

Pulmonary vein isolation (PVI) became an accepted therapeutic strategy for drug-resistant atrial fibrillation (AF) [1]. The cryoballoon (CB) ablation system was introduced into clinical practice as a tool for a single-shot anatomical based-PVI [2,3], and a comparable efficacy of CB ablation to radiofrequency (RF) ablation was demonstrated in a prospective randomized study [4]. The recently introduced second-generation CB (Arctic Front Advance, Medtronic, Minneapolis, MN) has been widely accepted owing to the high efficacy [4–7]. Because of the enhanced cooling effect, several recent studies have shown the feasibility of a single short freeze strategy with a single 28-mm balloon to minimize the risk of complications [8–10].

Over the decade, PV stenosis has been a well-recognized complication of AF ablation. PV stenosis has been described for both point-by-point RF ablation as well as CB ablation [1]. The incidence might be somewhat lower with CB ablation than with RF ablation [1], however, little data are available regarding PV stenosis after second-generation CB ablation using the current single short freeze strategy. The present study aimed to explore the incidence and predictors of PV stenosis after the second-generation CB ablation using a single 28-mm balloon and single short freeze strategy in a large patient series.

2. Methods

2.1. Study population

This study consisted of 276 consecutive patients with AF who underwent a PVI using a second-generation CB. In all patients, the PVI was performed exclusively with a 28-mm CB and single 3-minute freeze strategy (without any bonus applications after the isolation) [8]. Contrast enhanced cardiac computed tomography (CT) was obtained before (baseline) and >3 months after the procedure in all patients, and further follow-up CT was performed in patients with any PV stenosis. AF was classified according to the latest guidelines [1]. All patients gave their written informed consent. The study protocol

* Corresponding author at: Department of cardiovascular medicine, Fukui University, 23-3 Shimo-aiduki, Matsuoka, Eiheiji-cho, Yoshida-gun, Fukui 910-1193, Japan.
E-mail address: mshinsuke@k3.dion.ne.jp (S. Miyazaki).
[1] Cardiovascular Center, Tsuchiura Kyodo Hospital, Tsuchiura, Ibaraki, Japan.
[2] Heart Rhythm Center, Tokyo Medical and Dental University, Tokyo, Japan.

https://doi.org/10.1016/j.ijcard.2018.08.004
0167-5273/

was approved by the hospital's institutional review board. The study complied with the Declaration of Helsinki.

2.2. Mapping and ablation protocol

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 moderate sedation obtained with dexmedetomidine. A 100 IU/kg body weight of heparin 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). The transseptal sheath was exchanged over a guidewire for a 15-Fr steerable sheath (Flexcath Advance, Medtronic). A spiral mapping catheter (Achieve, Medtronic) was used to advance the 28-mm second-generation CB into the PV for support and to map the PV potentials. A 23-mm CB was not used in any cases. Following the verification of complete sealing with a contrast medium injection, a freeze cycle of 180 s was applied. All the CB applications were applied under monitoring the bilateral electromyography monitoring to anticipate phrenic nerve injury. The appropriate pacing site was carefully identified in the right and left subclavian veins with a deflectable quadripolar catheter. If the balloon temperature reached −60 °C or the amplitude of electromyography significantly decreased, the freezing was terminated with passive deflation (single stop) and active deflation (double stop), respectively. The procedural endpoint was defined as an electrical PVI, and no bonus applications were performed after the isolation. Additional touch-up ablation was performed if deemed necessary.

2.3. Definition of PV stenosis

Cardiac enhanced CT was performed with a 320-row scanner (Aquilion one, Toshiba, Otawara) prior to and >3 months after the procedure in all patients. Reconstructions were performed with a FC13 to generate 0.5-mm-thick slices with a reconstruction interval of 0.5 mm with a workstation (SYNAPSE VINCENT, Fujifilm, Tokyo). The PV ostium was defined as the point of inflection between the LA wall and PV wall. The PV ostial diameter was measured on the axial plane (anterior-posterior dimension) and coronal plane (superior-inferior dimension) for an optimal evaluation of the PV stenosis. PV stenosis was categorized as mild (25–50%), moderate (50–70%), and severe (>70%) according to the latest guidelines [1]. When any stenosis was detected, follow-up CT was further performed to evaluate the progression of the stenosis. All patients were evaluated for clinical symptoms such as a cough, dyspnea, and hemoptysis.

2.4. Follow-up

No antiarrhythmic drugs were prescribed after the procedure. The patients underwent continuous, in-hospital ECG monitoring for 2–3 days following the procedure. Subsequently, a 14 consecutive day monitoring using an external loop recorder (Spider Flash, Sorin, France) was undertaken following discharge. The first outpatient clinic visit was 3 weeks after the procedure. Subsequent follow-up visits consisted of a clinical interview, ECGs, and 24 h Holter monitoring every 3 months at our cardiology clinic. Patients with palpitations were encouraged to use a patient activated event recorder for one month. Recurrence was defined as any atrial tachyarrhythmias lasting longer than 30 s along the latest guidelines. Procedural success was defined as freedom from any recurrence without any antiarrhythmic drugs administered.

2.5. 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

The baseline patient characteristics are summarized in Table 1. In 276 patients, a total of 1101 PVs including 11 left common PVs (LCPVs) and 8 right middle veins were identified. Overall, 1067 of 1101 (96.9%) PVs were isolated successfully using exclusively 28-mm CBs, while the remaining 34 (3.1%) PVs (5 left superior PVs [LSPVs], 4 left inferior PVs [LIPVs], 3 right superior PVs [RSPVs], and 22 right inferior PVs [RIPVs]) required touch-up ablation. In total, all 1101 PVs were successfully isolated. The total number of CB applications per patient was 5.1 ± 1.4, and the mean number of CB applications was 1.2 ± 0.6, 1.2 ± 0.5, 3.3 ± 1.3, 1.1 ± 0.4, and 1.5 ± 0.8 for the LSPV, LIPV, LCPV, RSPV, and RIPVs, respectively. The total CB application time was 216 ± 104, 205 ± 77, 547 ± 223, 186 ± 68, and 246 ± 142 s for the LSPV, LIPV, LCPV, RSPV, and RIPVs, respectively. The nadir balloon temperature was −51.3 ± 5.4, −45.7 ± 4.8, −55.3 ± 4.6, and −52.4 ± 6.6 °C for the LSPV, LIPV, RSPV, and RIPVs, respectively. In 35 PVs (4 LSPVs, 2 LIPVs, 26 RSPVs, 3 RIPVs), freezing was abruptly interrupted by a double-stop technique due to suspected phrenic nerve injury, any patient symptoms, or a system error. Cardiac tamponade requiring pericardiocentesis and transient right phrenic nerve injury occurred in 1 and 7 patients, respectively. The total procedure and total fluoroscopic times were 78.1 ± 28.0 and 23.0 ± 13.6 min, respectively. A single procedure AF freedom without antiarrhythmic drug therapy was 73.4%.

Table 1
Patient characteristics.

N	276
Age, y	62.2 ± 11.0
Paroxysmal AF, n (%)	246 (89.1%)
Female, n (%)	72 (26.1%)
Structural heart disease, n (%)	18 (6.5%)
Body mass index, kg/m^2	24.4 ± 3.2
LA diameter, mm	37.6 ± 5.3
LV ejection fraction, %	65.9 ± 7.2
Pro-brain natriuretic peptide, pg/mL	308 ± 833
Anomaly	
Left common PV, n (%)	11 (4.0%)
Right 3 PVs, n (%)	8 (2.9%)
PV diameter on computed tomography	
LSPV diameter (coronal), mm	17.1 ± 2.6
LSPV diameter (horizontal), mm	13.4 ± 2.6
LIPV diameter (coronal), mm	14.7 ± 2.1
LIPV diameter (horizontal), mm	9.7 ± 2.5
RSPV diameter (coronal), mm	17.5 ± 2.6
RSPV diameter (horizontal), mm	14.2 ± 2.6
RIPV diameter (coronal), mm	16.1 ± 10.6
RIPV diameter (horizontal), mm	12.0 ± 2.8

AF: atrial fibrillation, LA: left atrial, LV: left ventricular, PV: pulmonary vein, LSPV: left superior PV, LIPV: left inferior PV, RSPV: right superior PV, RIPV: right inferior PV.

3.2. PV stenosis

In all 276 patients, cardiac CT was performed at a median of 5.0 [3.3–7.0] months after the initial procedure. No PVs exhibited any moderate or severe PV stenosis defined along the latest consensus statement guidelines [1]. Mild PV stenosis was documented in a total of 16 (1.4%) PVs, including 5 LSPVs, 5 LIPVs, and 6 RSPVs, among 14 (5.1%) patients (Fig. 1). On the contrary, no PV stenosis was observed in the RIPVs, LCPVs, and right middle veins. All 16 PVs were isolated by a sole CB without requiring any touch-up ablation. No patients had any symptoms related to PV stenosis, and no progression of the PV stenosis was observed on the follow-up CT in any of the PVs with mild stenosis.

There was no significant difference in the baseline patient characteristics between the 14 patients with mild PV stenosis and remaining 262 patients without any stenosis (Table 2). No stenosis was detected in the 35 PVs in which freezing was abruptly interrupted during the application. Although the number of PVs with any stenosis was extremely low, the potential parameters associated with stenosis (baseline PV diameter, nadir balloon temperatures, number of applications, and total freezing times) were compared between the PVs with and without mild stenosis. In the analysis, a longer cryoapplication time was the sole significant factor associated with mild RSPV stenosis, while no other factors predicted PV stenosis (Table 3).

4. Discussion

The present study investigated 1101 PVs that were targeted by a 28-mm second-generation CB using a single short freeze strategy, to

Please cite this article as: S. Miyazaki, et al., Does second-generation cryoballoon ablation using the current single short freeze strategy produce pulmonary vein stenosis? Int J Cardiol (2018), https://doi.org/10.1016/j.ijcard.2018.08.004