



Original article

Characteristics of dormant pulmonary vein conduction induced by adenosine triphosphate in patients with atrial fibrillation undergoing cryoballoon ablation



Kaoru Okishige (MD, FACC)^{a,*}, Hideshi Aoyagi (MD)^a, Takuro Nishimura (MD)^a, Takatoshi Shigeta (MD)^a, Tomofumi Nakamura (MD)^a, Yasuteru Yamauchi (MD)^a, Takehiko Keida (MD)^b, Tetsuo Sasano (MD)^c, Kenzo Hirao (MD)^c

^a Heart Center, Japan Red Cross Yokohama City Bay Hospital, Yokohama, Japan

^b Cardiology, Edogawa Hospital, Tokyo, Japan

^c Arrhythmia Center, Tokyo Medical and Dental University, Tokyo, Japan

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ABSTRACT

Background: Adenosine triphosphate (ATP) can provoke acute reconnections after pulmonary vein isolation (PVI). This study aimed to investigate dormant conduction (DC) after ablation with second-generation cryoballoon (CB).

Methods: Two hundred sixteen patients (148 male; age 64 ± 9 years) with atrial fibrillation (AF) were included. After a successful PVI with the CB, 20 mg of ATP was administered. All patients were followed up for 425 ± 56 days.

Results: Seven hundred ninety-five out of 864 (92%) PVs were successfully isolated solely by the CB. DCs were revealed in 8 (3.7%) after ATP injections. AF recurrences occurred in 2 out of 8 patients, while no AF recurrences could be documented in 6 out of 8 patients with DCs after a blanking period of 3 months (25% vs. 75%). In contrast, 29 (13.9%) patients without DCs had AF recurrences, and there was no significant difference between those with and without DCs regarding the recurrence rate of AF ($p = 0.38$). There were no reliable predictors of DCs after the PVI with the CB.

Conclusion: The present study demonstrated a low rate of transient PV reconnection after adenosine infusion following successful PVI with the CB. There was no reliable predictor of DCs.

Further studies will be needed in order to appreciate the prognostic value of adenosine testing after successful PVI with the CB.

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Introduction

Cryoballoon (CB) ablation is regarded as an effective technique with acute procedural success in more than 90% of patients with atrial fibrillation (AF) [1,2]. After the CB ablation, pulmonary vein (PV) reconnections may occur as dormant conduction (DC) transiently revealed by an infusion of adenosine [3]. The incidence of DC after CB ablation has been reported to range from 4% to 8% of PVs [4,5]. Although studies regarding the first-generation CB have shown a relatively low prevalence of this phenomenon [4,6], few data are available with the second-generation CB [5,7,8]. It is still

unclear what the clinical implication of the DC is for cryothermal ablation. The aim of this study was to assess the incidence of DC following a successful PV isolation (PVI) and to identify the potential predictors of DC using the CB.

Methods

Patient population

The study protocol was approved by the local Institutional Committee on Human Research at our institution. Two hundred sixteen consecutive patients with drug-refractory AF eligible for PVI using the CB were included. All patients underwent a CT-scan prior to the ablation to establish the left atrial (LA) and PV anatomy. All patients provided informed consent prior to the ablation procedure. Exclusion criteria included continuous AF for >2 years,

* Corresponding author at: Heart Center, Yokohama-city Bay Red Cross Hospital, 1-12-3 Shinyamashita, Naka-ward, Yokohama 231-8682, Japan.
E-mail address: okishige@yo.rim.or.jp (K. Okishige).

an LA size >55 mm, intracardiac thrombi, and uncontrolled heart failure. The study complied with the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee.

Pulmonary vein isolation procedure

An 8 Fr intracardiac echocardiography (ICE) catheter (Acuson, AcuNav, Biosense Webster, Diamond Bar, CA, USA) was introduced through the femoral vein and positioned in the right atrium. A decapolar catheter was placed in the coronary sinus. A single transeptal puncture was performed using a transeptal radio-frequency (RF) needle (NRG RF transeptal needle, Baylis Medical, Montreal, Canada) guided by both ICE and fluoroscopy. After gaining left atrial access, a 100 UI/kg heparin intravenous bolus was given. A steerable 15 Fr over-the-wire sheath (FlexCath, Medtronic, Minneapolis, MN, USA) was positioned in the LA. A circular mapping catheter (Achieve, Medtronic) was then advanced into each PV ostium. A 28 mm CB (Arctic Front Advance, Medtronic) was advanced over the wire up to the LA, and inflated and positioned in the PV ostium of each PV. Optimal vein occlusion was considered to have been achieved when a selective contrast injection exhibited total contrast retention with no flow to the atrium. The first cryoablation was performed for 3 min per application, and the second freezing was performed when a conduction gap (GAP) between the LA and PVs was found. A touch-up ablation using irrigated RF energy was undertaken when a GAP persisted despite the second freezing. All touch-up ablation sites were tagged on the endocardial surface of the LA and PVs by a NavXsystem (St. Jude Medical, Minneapolis, MN, USA), and those tagged sites were utilized for the comparison of the anatomical sites in the LA between the reconnections provoked by an intravenous bolus injection of adenosinetriphosphate (ATP) and the touch-up ablation. During the entire procedure, the activated clotting time was maintained over 300 s by a supplemental heparin infusion, as required.

Assessment of phrenic nerve injury

A quadripolar catheter was positioned in the left or right subclavian vein for continuous phrenic nerve (PN) stimulation during an ipsilateral cryo-application. Diaphragmatic stimulation was achieved by pacing the ipsilateral phrenic nerve with a 1500 ms cycle. The compound motor action potentials of the diaphragm (CMAP) provoked by the PN pacing were continuously monitored during freezing. In addition to the CMAP recordings, the PN function was also monitored continuously by palpation of the diaphragmatic excursions. CMAP recordings were obtained as reported previously [9,10]. The CMAP signals were recorded on a NavX recording system.

Assessment of the PV electrical isolation

PV activity recording was attempted with an Achieve catheter during the cryoablation procedure. A successful PVI was considered to have been obtained when all PV potentials were abolished or dissociated from the atrial activity, and bidirectional block was documented. Entry block of the PV activity was demonstrated using ATP for the PV while pacing from the distal coronary sinus. Exit block was verified by pacing from each bipolar pair of the mapping catheter in the PVs with the maximum output of the stimulator (Cardiac Stimulator: SEC-4103, Nihon Kohden, Tokyo, Japan).

Adenosine challenge for the evaluation of PV reconnections

Two circular mapping catheters were simultaneously positioned in the ipsilateral superior and inferior PVs for the recording

of PV potentials. Thirty minutes after the successful PVI only by cryo-freezing or by the additional touch-up RF ablation, 20 mg of ATP was intravenously injected during an isoproterenol infusion (2 μ g/min) starting from left-sided PVs then moving to the right-sided ones. When a transient LA-PV reconnection was documented, an RF irrigated ablation catheter (Thermocool, Biosense Webster) was used to target the earliest activation site identified on the circular multipolar catheter (Liberio, Japan Life Line, Tokyo, Japan).

Definitions

Spontaneous PV reconnections were defined as the incidence of an LA-PV reconnection during the 30-min waiting period following the final successful PVI procedure. The ATP-induced PV reconnections consisted of the reappearance of the LA-PV conduction by an ATP challenge after a 30-min waiting period. The nadir temperature was the lowest temperature reached during the cryoenergy application.

Follow-up

After discharge, all patients were scheduled for a physical examination with a baseline electrocardiogram and 24 hour Holter recording examination at 1, 2, 4, 6, 8, 10, and 12 months after a blanking period of 3 months following the ablation procedure. All documented AF episodes of >30 s were considered as a recurrence. All patients with an AF recurrence underwent a re-do session with an irrigated RF energy system after a blanking period of 3 months.

Statistical analysis

The continuous variables are expressed as the mean \pm standard deviation. Continuous and categorical variables were compared with a Student's *t*-test and chi-square test, respectively. A probability value of $p < 0.05$ indicated statistical significance.

Results

Study population

Two hundred sixteen patients (148 males; mean age 64 ± 9 years) affected by drug-resistant paroxysmal (188/216, 87%) or early persistent (29/216, 13%) AF (defined as AF lasting shorter than 3 months), undergoing ablation with only a 28 mm CB, were included into the study. All patients failed at least > 1 class I or III antiarrhythmic agent prior to the ablation.

The patients were divided into 2 groups: 8 (3.7%) patients with any acute reconnections that were provoked by ATP (**Group A**) during a 10-second period, and 208 patients (96.3%) without any reconnections provoked by adenosine (**Group B**). The study population's baseline clinical and echocardiographic procedural characteristics are depicted in [Table 1](#).

Procedural characteristics

The mean total procedure time and fluoroscopic time were 123.6 ± 18.7 min and 21.8 ± 8.7 min, respectively, including the observational time and ATP challenge. It was possible to map all PV ostia, which were recognized by the venography of each PV, and the PV potentials were present in all PV ostia before the ablation. Four left-sided common ostia were found, and the CB was not applied in those cases. A successful occlusion could be obtained in 812 (94%) PVs. In 13 patients, we performed a second CB application because an optimal occlusion could not be reached with the first CB application. Real-time recordings of the PVs during the freezing could be observed in 65% of the left superior

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