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Optimal observation time after completion of circumferential pulmonary vein isolation for atrial fibrillation to prevent chronic pulmonary vein reconnections

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ABSTRACT

Purpose: To identify predictors of chronic pulmonary vein (PV) reconnection (CPVR) after successful circumferential PV isolation (CPVI) for atrial fibrillation (AF).
Materials and methods: A total of 718 PVs from 181 consecutive AF patients (141 males, median age 61 years, 92 paroxysmal AF) who underwent a second ablation procedure for recurrent AF were retrospectively analyzed.
Results: During the second procedure, a CPVR was observed in 477 PVs (66.4%) among 169 patients. In a multiple logistic regression analysis, the observation time after the final completion of the PVI (OT-final) was a significant negative predictor (odds ratio 0.980; $P < 0.001$). A receiver operating characteristic analysis demonstrated that the greatest area under the curve was for the OT-final (0.670). At an optimal cutoff of 35 min, the sensitivity and specificity for predicting a CPVR were 66.9% and 60.6%, respectively. By Kaplan Meier analysis, CPVR was more frequent in PVs with an OT-final of <35 min than ≥35 min (log-rank test, $P = 0.018$). In a vessel-by-vessel analysis, the OT-final at all PV sites was a significant negative predictor, while male gender in the right PVs and left-inferior PV, number of RF applications for the ipsilateral CPVI in the right PVs and left-superior PV, and major PV diameter in the left-superior PV were significant positive predictors of a CPVR (all $P < 0.05$).
Conclusions: An optimal observation time (≥35 min in this study) to determine whether PVI is successfully completed during the initial CPVI for AF may be needed to prevent a CPVR and subsequent AF recurrence thereafter.

1. Introduction

Radiofrequency (RF) catheter ablation is used as a curative treatment for drug-refractory atrial fibrillation (AF). Pulmonary vein (PV) isolation (PVI) is widely performed as the mainstay of RF catheter ablation of paroxysmal AF [1–6]. It is known that AF recurrence after PVI in patients with paroxysmal AF is often associated with recovery of conduction between the PVs and the left atrium (LA) [7–9]. Thus, multiple sessions of PVI improve the success rate in treating paroxysmal AF [4,7]. PVI alone is not as effective in persistent or long-standing persistent AF as in paroxysmal AF [10,11], whereas circumferential PVI (CPVI) has been reported to be sufficient to restore sinus rhythm in 43.2% of patients with long-standing persistent AF [12]. Furthermore, PVI combined with additional substrate modification for AF improves the success rate in treating persistent or long-standing persistent AF, compared with PVI alone [11,13]. Therefore, PVI has emerged as the cornerstone of AF ablation not only in paroxysmal AF but also in persistent or long-standing persistent AF.

The goal of PVI is to achieve a bidirectional conduction block between the PVs and the LA and to permanently maintain this PV–LA conduction block. Nevertheless, PV reconnection (PVR) is relatively common not only acutely but also chronically after successful PVI by RF catheter ablation [4,14–17]. Therefore, minimizing the occurrence of chronic PVR (CPVR) after PVI may contribute to a reduction in the number of sessions of AF ablation required and in the subsequent likelihood of AF recurrence. However, the factors predicting a CPVR after a successful PVI for AF have not yet been fully elucidated.

The purpose of the present study was to identify the predictors of a CPVR after an initially successful CPVI for AF.

2. Materials and methods

2.1. Study population

A total of 181 consecutive patients with AF (141 males, median age 61 years) who underwent a second ablation procedure for recurrent AF after a first RF catheter ablation of AF were retrospectively studied. Both the first and second ablation procedures in all patients were performed at our institute between April 2009 and February 2013. Patients with previous surgical LA ablation were excluded from the study. In 3 of the 181 AF patients studied, 3 pairs of each-sided superior and inferior PVs (a total of 6 PVs), including 2 pairs of right-sided superior and inferior PVs and 1 pair of left-sided superior and inferior PVs were excluded from the analysis because in 2 patients each had 1 PV that originally

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had no PV potential (1 right inferior PV (RIPV) and 1 left inferior PV (LIPV)), and the remaining patient had 1 RIPV which could not be completely isolated during the first procedure. Thus, a total of 718 PVs from the 181 AF patients were analyzed.

2.2. Enhanced multislice CT imaging and echocardiography before ablation

The day before the procedure, all patients underwent contrast-enhanced electrocardiogram (ECG)-gated multislice computed tomography (CT) (Light Speed Ultra, General Electric, Milwaukee, WI, USA or SOMATOM Definition, Siemens Medical Solutions, Forchheim, Germany) for assessment of the PV and LA anatomy using three-dimensional (3D) reconstruction. Data sets were reconstructed using a retrospective ECG-gating technique and image reconstruction was performed at 70% of the ECG R-to-R intervals. In the virtual endoscopic views of 3D perspective volume-rendered CT images, the major and minor diameters of each PV were measured by an experienced radiologist without knowledge of the baseline characteristics. Furthermore, using an electroanatomic mapping system (CARTO, Biosense Webster, Diamond Bar, CA, USA), the 3D CT images were integrated into the electroanatomic maps in order to provide a real-time representation of the cardiovascular structures during the ongoing ablation procedure.

All patients underwent transthoracic echocardiography to assess the LA and left ventricular (LV) sizes and LV function using standard parasternal and apical views and transesophageal echocardiography to rule out intracardiac thrombi before the procedure. Written informed consent was obtained from all patients for all examinations.

2.3. Electrophysiological study and radiofrequency ablation procedure

Written informed consent for the electrophysiological study and RF catheter ablation of AF was obtained from all patients. Antiarrhythmic drugs were discontinued at least five half-lives before the procedure, with the exception of amiodarone and bepridil which were continued during the procedure in most of the patients. A total of 173 patients (95.6%) received oral anticoagulant therapy using warfarin ($n = 152$) or dabigatran ($n = 21$) prior to the first procedure. Warfarin was continued throughout the procedure and dabigatran was discontinued on the day of the procedure and resumed the day after [18]. All patients received conscious sedation during the procedure using propofol or dexmedetomidine, and pentazocine.

A deflectable multielectrode catheter was positioned in the coronary sinus via the right femoral vein. A transseptal puncture was made under the guidance of a right atriogram and fluoroscopy. After the transseptal puncture, a 5000-unit bolus of heparin was administered, followed by a continuous and additional bolus infusion of heparin to maintain an activated clotting time of 300 to 350 s, which was checked every 30 min throughout the procedure. Three 8-French long sheaths (SL0, St. Jude Medical, St. Paul, MN, USA) were advanced into the LA over one transseptal puncture site. An ablation catheter and two 7-French decapolar circular mapping catheters (Lasso, Biosense Webster or RIVERO, Japan Lifeline Co., Ltd., Tokyo, Japan) were introduced into the LA through the long sheaths. Each PV ostium was identified by selective PV angiography and electrophysiologically and two circular mapping catheters were positioned at the ostia of the ipsilateral superior and inferior PVs. Surface ECGs and intracardiac electrogram recordings from the coronary sinus and circular mapping catheters were stored digitally on either an EP-WorkMate system (EP Medical Systems, Mount Arlington, NJ, USA) or Bard EP LabSystem (Bard Electrophysiology, Lowell, MA, USA). The bipolar electrograms were filtered between 30 and 500 Hz. In order to minimize the risk of esophageal injury, fluoroscopic imaging of the esophagus using contrast medium to identify the course of the esophagus and/or esophageal temperature monitoring using an esophageal temperature probe (SensiTherm, St. Jude Medical) was performed during the procedure.

During the first ablation procedure, CPVI was performed in all patients and additional substrate modification for AF in the LA and right atria, including complex fractionated atrial electrogram ablation and/or linear ablation, was performed if the spontaneous or induced AF did not cease after the CPVI. Non-PV foci triggering AF were also ablated if present. RF ablation along the CPVI line was performed by a point-by-point ablation technique using a 3.5-mm-tip open-irrigated ablation catheter (NaviStar ThermoCool or EZ Steer ThermoCool, Biosense Webster) guided by a double Lasso technique and 3D electroanatomic mapping system (CARTO XP or CARTO 3, Biosense Webster, Diamond Bar, CA, USA). The continuous circumferential lesions were created to extensively encircle the ipsilateral superior and inferior PVs 5 to 10 mm outside their ostia. At the anterior aspect of the left PVs (LPVs), RF ablation was performed along the ridge between the LPVs and the LA appendage. All RF sites were tagged onto the 3D CT reconstructions integrated into the electroanatomic maps using an image integration software module (CARTO Merge, Biosense Webster, Diamond Bar, CA, USA). Each application of RF energy was delivered for 40 to 50 s with a power of up to 35 W, maximum temperature of 41 °C, and irrigated flow rate of 17 or 30 ml/min using a Stockert RF generator (Biosense Webster, Diamond Bar, CA, USA). RF energy deliveries to sites at the LA posterior wall close to the esophagus were limited to a maximum power of 25 W and RF energy delivery duration of up to 30 s. In patients with esophageal temperature monitoring, a temperature limit of 41 °C was defined as the cut-off to interrupt RF energy deliveries. At first, a right-sided and then left-sided CPVI was achieved during sinus rhythm, distal coronary sinus pacing, or AF. Additional RF applications slightly inside the CPVI line were performed when a PVI could not be successfully completed with the initial circumferential ablation. Thereafter, elimination or dissociation of all PV potentials was determined during sinus rhythm or AF. Electrical cardioversion restored sinus rhythm if AF did not cease after the CPVI of both the right and left PVs and additional substrate modification for AF. Bidirectional conduction block between the PVs and the LA was verified in all the PVs, as indicated both by the elimination or dissociation of the PV potentials recorded by the circular mapping catheter (entrance block) and failure to capture the LA by pacing from each bipolar pair of the mapping catheter at the PV ostium (exit block). If recovery of conduction between the PVs and the LA occurred, any reconnected PV was re-isolated by additional RF applications and bidirectional PV–LA conduction blockade was performed again. Furthermore, in 566 PVs (78.8%) from 146 patients, dormant PV conduction was provoked by intravenous administration of 10–20 mg adenosine triphosphate (ATP) together with a continuous infusion of isoproterenol at 1–2 μg/min during coronary sinus pacing and was then eliminated by additional RF applications if it was detected [19–21]. Finally, lack of stimulation of dormant PV conduction by ATP was confirmed in all PVs with ATP-induced dormant PV conduction. At the end of the first procedure, PVI could be successfully completed in all the PVs.

2.4. Management and follow-up after the first procedure

Transthoracic echocardiography was performed after the procedure to rule out any pericardial effusions. Intravenous administration of 10,000 to 20,000 units of heparin per day was continued for at least 24 h after the procedure, followed by oral anticoagulant therapy with warfarin or dabigatran for at least 3 months in all patients. The decision to discontinue antiarrhythmic drugs was left to the patient's physician in consultation with the individual electrophysiologist performing the procedure. All patients were followed up in outpatient clinics every 1 to 2 months after the first procedure. AF recurrence after the first procedure was documented by 12-lead ECG or 24-h Holter monitoring at each follow-up or emergency visit.

During the second ablation procedure, the presence or absence of a CPVR was assessed in each PV using a circular mapping catheter. All reconnected PVs were re-isolated and additional substrate modification and/or ablation targeting non-PV foci was performed if spontaneous or induced AF did not cease and/or non-PV foci triggering AF could be identified after the second CPVI. If atrial tachycardia (AT) or flutter (AFL) was present, the AT/AFL was mapped and ablated.

2.5. Assessment of PVR and the procedural parameters during the first CPVI

The presence or absence of an acute PVR (APVR) and CPVR was assessed in all PVs during the first and second procedures. An APVR was defined as a PVR which occurred with or without intravenous administration of ATP from the initial completion of the PVI to the final check of the complete PVI, and was successfully eliminated by additional RF applications during the first procedure. A CPVR was defined as a PVR which was observed in the second procedure in PVs which were successfully isolated at the end of the first procedure. The procedural parameters associated with the first procedure were also evaluated, including the procedural time (minutes), total ablation time (seconds), number of RF applications, and total RF energy delivery (J) required for the ipsilateral CPVI, heart rhythm during the ipsilateral CPVI (sinus rhythm or AF), and presence or absence of provocation of dormant PV conduction by ATP. The patterns of the PVI were classified into the following two groups: one pattern was a simultaneous isolation of both the superior and inferior PVs on each side and the other pattern was an individual isolation of the superior and inferior PVs on each side. A left common PV was seen in 19 patients and isolated at the common PV trunk in those patients. The isolation of the left common PV was regarded as a simultaneous isolation of the LPVs. In addition, the observation times (minutes) from the initial completion of the PVI to the final check of the complete PVI (OT-initial) and from the final completion of the PVI to the final check (OT-final) were recorded. If the PVs had no APVR, the OT-initial was equal to the OT-final. On the other hand, if the PVs had an APVR which was eliminated by additional RF applications, the OT-initial was longer than the OT-final in those PVs.

2.6. Statistical analysis

Normally-distributed continuous variables were expressed as the mean ± standard deviation (SD) and non-normally distributed continuous variables were expressed as the median and interquartile range (IQR, 25th–75th percentile). A comparative analysis was performed using Student's t-test for normally distributed continuous variables and Mann–Whitney's U-test or Kruskal–Wallis test for non-normally distributed continuous variables. Categorical variables were expressed as absolute values and percentages and a comparative analysis was performed using a chi-squared test. The PVs were classified into four categories according to the site: right superior PV (RSPV), RIPV, left superior PV (LSPV), and LIPV. Logistic regression models were generated for all PVs and for each PV site to identify the predictors of a CPVR, using the age (years), gender, body mass index (kg/m^2), AF duration (months), presence of structural heart disease, serum brain natriuretic peptide (BNP) level (pg/ml), PV and LA diameters (mm), site of the PVs (RSPV, RIPV, LSPV, or LIPV), heart rhythm during the ipsilateral CPVI (sinus rhythm or AF), observation time after completion of the PVI (minutes), simultaneous isolation of the ipsilateral PVs, provocation of dormant PV conduction by ATP, and the procedural time (minutes), total ablation time (seconds), number of RF applications, and total RF energy delivery (J) of the ipsilateral CPVI. To compare the strength of the association of these parameters with prediction of CPVR in all PVs, the area under the receiver operating characteristic (ROC) curve for each parameter was estimated. A Kaplan–Meier analysis and log-rank test were used to evaluate the event-free survival rate from a CPVR after the first ablation procedure. $P < 0.05$ was considered to be statistically significant. The statistical analyses used SPSS Statistics 20 software (SPSS, Inc., Chicago, IL, USA).