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Original article

Lessons from individualized cryoballoon sizing. Is there a role for the small balloon?

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ABSTRACT

Background: Cryoablation for paroxysmal atrial fibrillation (PAF) is well established. The single-big-balloon strategy has been preferred for pulmonary vein isolation (PVI) using the second generation cryoballoon (CBG2). Individual PV-morphologies raise the question if an individualized anatomic approach using the 23-mm or 28-mm CB is reasonable.
Methods: Consecutive patients were prospectively enrolled in the non-randomized single-center study. Patients were treated with the 28-mm CB, if any PV was >21 mm, the 23-mm CB, if all PV were ≤21 mm, or both sizes, if PVI was difficult. The primary endpoint was arrhythmia-free survival. The secondary endpoint considered procedural results and complications.
Results: Overall, 197 patients with symptomatic PAF (64 ± 11 years, 36% female) were included. Acute PVI was achieved in 99.9% of PV. Based on preprocedural imaging, the 28-mm CB was applied as the primary catheter in 47% (92/197 patients), the 23-mm CB in 53% (105/197, $p = 0.23$). The 23-mm CB group included more females, patients with short left atrial (LA)-diameters (each $p < 0.01$), and smaller patients ($p = 0.04$). Both CB-sizes were used in 24% (47/197). Additional 23-mm CB usage was necessary in 23% (21/92) of patients, mainly because of insufficient PV-occlusion with the 28-mm CB. Additional 28-mm CB usage was necessary in 25% (26/105, $p = 0.82$), mainly because PV diameters were larger than initially measured. Both CB-sizes were equally safe and effective with a low complication rate and an overall success rate of 86% at 12 and 71% at 18 months (6% on antiarrhythmic drugs). No predictors for AF-recurrence were identified.
Conclusion: CB ablation can sometimes be challenging. The 28-mm CB is the preferred catheter in all patients. If balloon positioning is difficult, the 23-mm CB is an option to achieve PVI in small veins. Further studies need to investigate if the 23-mm CB could be beneficial as the primary CB in females with small body height and short LA diameter.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia associated with a reduced quality of life, increased morbidity and mortality [1]. According to the current guidelines, catheter ablation for pulmonary vein isolation (PVI) is recognized as a class I/A indication for the treatment of symptomatic drug-refractory paroxysmal (P)AF [1,2]. The second-generation cryoballoon (CBG2, Arctic Front Advance; Medtronic Inc, Minneapolis, MN, USA) has attracted worldwide interest as an effective and safe ablation tool. Consistent results regarding safety, procedural efficacy [3,4], and clinical outcome were published by different groups using a single-big balloon approach (28-mm CBG2 only) and freedom from arrhythmia was seen in 80% and more after one year [5–8]. However, in some patients the ablation with the big cryoballoon only can be challenging because of the variety of different PV morphologies and especially in small and inferior veins. We evaluated the safety and efficacy of CBG2-PVI based on an individualized anatomic approach using the 28-mm, the 23-mm, or both balloons for a large group of consecutive patients with symptomatic PAF undergoing AF ablation as an index procedure.

Methods

Objectives

The purpose of the study was: (1) to evaluate the clinical outcome ≥12 months after primary cryoballoon ablation and individual CB

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size selection in a large consecutive group of patients with PAF, (2) to analyze procedural data and periprocedural adverse events.

Study population

Consecutive patients with PAF who underwent PVI with CBG2 as an index procedure and who were eligible for a follow-up ≥ 12 months were prospectively enrolled in our non-randomized, single-center observational registry study. PAF was defined as classified in the current guidelines [1]. Patients were diagnosed with symptomatic drug-refractory PAF or had contraindications for antiarrhythmic drug (AAD) treatment. According to the guidelines, the wish of selected patients was considered in the decision for PVI as the primary AF therapy (class II a/B recommendation) [1]. Exclusion criteria were persistent AF, prior AF ablation therapy, intracardiac thrombi, and severe valvular disease. All patients provided written informed consent for participating in the study prior to ablation therapy. The study was approved by the institutional review committee and complies with the declaration of Helsinki.

Ablation procedure protocol

A detailed summary of our standardized ablation procedure has been previously described [3,9]. Cardiac computed tomography (CT) or magnetic resonance imaging (MRI) scanning was performed in all patients prior to ablation to build a 3D reconstruction of the left atrial (LA)/PV-anatomy, and to rule out significant coronary heart disease if the coronary status was not evaluated before [10]. Intracardiac thrombi were ruled out using transesophageal echocardiography. PVI was performed with the 28-mm and/or the 23-mm cryoballoon (CBG2) as necessary to isolate all PVs sufficiently. After advancing the balloon into the left atrium through a single intracardiac echocardiography (ICE)-guided transseptal puncture (Vivid I, GE Healthcare EUROPE, GE Ultraschall Deutschland GmbH, Solingen, Germany) in an over-the wire technique the balloon was inflated and positioned at the PV ostium. The 8-pole spiral mapping catheter (15 or 20 mm Achieve™, Medtronic Inc.) was used for balloon positioning, mapping, and real-time-PV potential recording. The degree of vessel occlusion was assessed by PV angiography immediately prior to ablation. Then, refrigerant supply was started and PVI was performed with at least two freeze-thaw-freeze cycles per vein including one bonus application after acute electrical isolation. The standard freezing time was ≥180 and ≤240 seconds. The temperature limit was set minus 55 °C CB-temperature for right-sided PVs. ICE was used in all cases to verify optimal antral balloon positioning at the PV ostium and vessel occlusion (Doppler imaging) during ablation. PV-potentials were mapped before and after each freeze cycle and 15 minutes after the last freeze. One bonus application was applied after acute PVI was achieved. Time to isolation was determined if PV potentials were visible during the cryoapplication. The use of the second balloon size or touch-up applications (RF- or cryotip-catheters) was allowed to obtain PVI. RF ablation was only used if PVI was not achievable using cryoenergy. During the entire procedure, intravenous heparin was administered to maintain an activated clotting time between 300 and 400 seconds. Before sheath removal, protamine was given to reduce the risk of bleeding. One hour after sheath removal, we continuously administered intravenous unfractionated heparin with a target partial thromboplastin time of 50 to 70 seconds and oral anticoagulation was resumed on the day after ablation.

Cryoballoon size selection

Patients were primarily treated with the 28-mm CB, if any PV was >21 mm. The 23-mm CB was used as the primary catheter, if all PV were exclusively small (≤21 mm). If PVI could not be achieved with the first balloon, e.g. because of insufficient occlusion with the 28-mm CB, or, when the 23-mm CB was too small for one of the veins (intraprocedural guidance using angiography or ICE to ensure antral balloon positioning), the other CB size (23-mm or 28-mm CB) was applied as a second catheter. However, the 23-mm CB was only allowed in those veins with a PV diameter ≤21 mm to prevent too distal balloon deployment within the PV [11].

Phrenic nerve monitoring

For the early recognition of possible phrenic nerve palsy (PNP), continuous phrenic nerve pacing with a cycle length of 1200 ms was performed after achieving −20 °C or 20 seconds of freezing time using a 4-pole deflectable catheter placed near the junction of the superior vena cava (SVC) and the right subclavian vein or the anterolateral portion of the SVC, near the atrial-SVC junction, and continuous palpation of the diaphragm was performed. Cryoenergy was immediately interrupted if weakening or loss of diaphragmatic contractions were noticed.

Esophageal temperature probe

An esophageal temperature probe (SensiTherm™, 3 thermocouples, St. Jude Medical, Saint Paul, MN, USA) was used in all patients to detect the lowest esophageal temperature. Cryoenergy was immediately terminated if the intraluminal esophageal temperature reached ≤+15 °C. This cut-off value is based on recent findings demonstrating that an esophageal temperature ≤+12 °C induced esophageal lesions with 100% sensitivity and 92% specificity [12], and our own observation that there is always a further temperature drop after the termination of the freeze.

Follow-up

Electrocardiography (ECG) and Holter studies were performed for the first 24 to 48 hours post ablation and up to 7 days in patients with AF symptoms. Transthoracic echocardiography was performed in all patients to rule out pericardial effusion. All complications were registered prospectively. Routine outpatient follow-up was performed at 1, 3, 6, 12, and 18 months (Holter, ECG, symptoms). We collaborated with referring centers to confirm the diagnosis if any recurrence was suspected based on outpatient follow-up results.

Statistical analysis

Continuous data are given as mean with standard deviation (SD) or as the median with interquartile range (IQR), if data were non-normally distributed in accordance to the Kolmogorov–Smirnov test. Continuous data were compared using the Student's *t*-test, or, in case of more than two groups, using ANOVA test (analysis of variance) or Kruskal Wallis test, if appropriate. Categorical data are shown as numbers and percentages and were compared using the chi-square test. In case of more than two groups, further closed testing procedure was performed. Event rates were plotted over time using Kaplan–Meier method. Univariate and multivariate analyses were performed to ascertain potential predictors for AF recurrence using the Cox-regression model. A two tailed p-value < 0.05 was considered significant. Data processing and analysis was performed using Excel 2010 (Microsoft Corp., Redmond, WA, USA) and SPSS 20.0 (IBM Corp., Armonk, NY, USA).

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