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Original article

Clinical outcome of 2nd generation cryoballoon pulmonary vein isolation in patients over 75 years of age

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ABSTRACT

Background: Pulmonary vein isolation is an established therapy for symptomatic atrial fibrillation. Despite the fact that incidence and prevalence of atrial fibrillation increases with age, patients over 75 years of age have been excluded in all major atrial fibrillation ablation trials. Pulmonary vein isolation with the cryoballoon has been shown to be equally effective compared to irrigated radiofrequency catheter ablation, but patients over 75 years have also been excluded. The 2nd generation cryoballoon has shown superior efficacy compared to the 1st generation cryoballoon. The aim of the study was to assess the efficacy of pulmonary vein isolation with the 2nd generation cryoballoon for symptomatic atrial fibrillation in elderly patients over 75 years.

Methods: Patients over 75 years of age presenting with symptomatic paroxysmal or persistent atrial fibrillation refractory or intolerant to at least one class I or class III antiarrhythmic drug who underwent pulmonary vein isolation with the 2nd generation cryoballoon were included in this single-center observational study.

Results: A total of 40 patients with a mean age of 78.3 ± 2.7 years with paroxysmal (n = 31; 77.5%) or persistent (n = 9; 22.5%) atrial fibrillation were identified. All patients had a successful pulmonary vein isolation procedure with 100% of veins isolated. After a 3-month blanking period during a mean follow-up of 15.1 ± 8.2 months there were 9 (22.5%) arrhythmia recurrences, while 31 patients (77.5%) maintained stable sinus rhythm. Freedom from arrhythmia recurrence was 86.4% at 12 months and 80.2% at 24 months.

Conclusions: Pulmonary vein isolation with the 2nd generation cryoballoon appears to be an effective treatment for symptomatic atrial fibrillation also in patients over 75 years of age.

Introduction

The incidence and prevalence of atrial fibrillation (AF) are age-dependent. Under the age of 55 years, the overall prevalence is below 0.2% but increases to more than 5% in those aged over 75 years [1]. Pulmonary vein isolation (PVI) has become an established and effective treatment for drug-refractory AF. However, even though the elderly represent a large proportion of all patients suffering from AF, in most PVI studies such as MANTRA-PAF [2], STOP AF [3], and RAAFT-2 [4], patients over the age of 75 years have been excluded. This may be due to the concern that complications might be more common or more severe in the elderly or that success rates might be lower. Thus, efficacy of PVI in this large and important group of AF patients is largely unknown.

Cryoballoon PVI has been shown to be equally effective to irrigated radiofrequency catheter ablation for AF [5,6]. Recently, the 2nd generation cryoballoon (Arctic Front Advance, Medtronic Inc., Minneapolis, MN, USA) has been introduced, and has shown reproducibly good results with freedom from AF in 80 to 91% at 1-year follow-up in several studies of paroxysmal and early persistent AF [7–15]. At the same time, complication rates of PVI procedures with the cryoballoon are generally low, and mainly comprise transient phrenic nerve palsy. To date, no data on efficacy of PVI with the 2nd generation cryoballoon in patients over 75 years have been reported. The aim of this study is to assess the single-procedure outcome of PVI with the 2nd generation

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cryoballoon in a series of consecutive patients over 75 years of age presenting for symptomatic AF.

Methods

Study population

A consecutive series of patients over 75 years of age, who underwent PVI with the 2nd generation cryoballoon as treatment for paroxysmal (pAF) or persistent atrial fibrillation (perAF) between November 2012 and May 2015, were included in this single-center observational study and clinically followed. Patients had to be refractory or intolerant to at least one class I or class III antiarrhythmic drug (AAD) or AAD were refused as first-choice therapy by patients. Exclusion criteria were long-standing perAF, previous left atrial (LA) ablation, presence of LA thrombus on transesophageal echocardiography prior to the procedure, LA diameter >60 mm, uncontrolled heart failure [New York Heart Association (NYHA) class IV], moderate or severe valvular disease, acute coronary syndrome and/or percutaneous coronary intervention within one month before the procedure, frailty, and life expectancy of less than 1 year. The study complies with the Declaration of Helsinki and was approved by our institutional review committee. All patients gave written informed consent to the procedure.

Periprocedural management

All patients had transesophageal echocardiography before PVI to rule out intracardiac thrombi. No other imaging was obtained prior to the procedure. Patients on vitamin K-antagonists were scheduled for the procedure at a target international normalized ratio of 2.0–3.0. Similar to a recent report, patients on direct oral anticoagulants (dabigatran, apixaban, and rivaroxaban) were advised to take the last dose 24 h prior to the procedure [16]. No heparin bridging was given to any patient. Direct oral anticoagulants were continued on the evening of the day of the procedure. Anticoagulation was advised to be continued indefinitely, because based on the inclusion criteria, all patients had a CHA_2DS_2-VASc Score of at least 2. All patients underwent transthoracic echocardiography to rule out pericardial tamponade or pericardial effusion immediately after the procedure and prior to hospital discharge.

Cryoballoon ablation procedure

The procedure was performed under deep sedation using midazolam, fentanyl, and propofol. A diagnostic catheter was introduced via the right femoral vein and placed in the coronary sinus. Transseptal puncture was performed via the right femoral vein under fluoroscopic guidance using a Brockenbrough catheter and a 2H transseptal needle (Maslanka, Tuttlingen, Germany). A heparin bolus was administered targeting an activated clotting time >300 s. A guidewire was introduced into the left superior pulmonary vein (PV) and the Brockenbrough catheter was exchanged to a 12F steerable sheath (Flexcath advance, Medtronic). Selective PV angiography was recorded in order to identify all PV ostia. Subsequently, a 28 mm Arctic Front Advance cryoballoon was advanced to the LA via the transseptal sheath and with a 20-mm spiral mapping catheter (Achieve, Medtronic) as guidewire. The cryoballoon was inflated proximal to the PV ostium, advanced and pushed to the PV ostium aiming at complete sealing of the PV without advancing the balloon into the PV. Complete occlusion at the ostial/antral level was documented by injection of contrast medium through the central lumen of the cryoballoon. Complete occlusion was followed by a freeze cycle of 240 s. After successful PVI – documented by entry- and exit-block with the spiral mapping catheter – one additional bonus freeze cycle of 240 s was applied at each PV. A temperature probe (Sensitherm; St. Jude Medical Inc, St Paul, MN, USA) was transnasally advanced into the esophagus and placed at the closest possible proximity to the balloon during each ablation. A luminal esophageal temperature below 15 °C was used as a cut-off to trigger termination of the freeze cycle. Phrenic nerve function was monitored by phrenic nerve stimulation via the diagnostic catheter placed in the superior vena cava and palpation of the right-sided diaphragm, and in a subset of patients with additional recording of compound motor action potentials of the right-sided diaphragm by surface electrocardiogram (ECG) [17,18].

Follow-up

Patients were scheduled for outpatient clinic visits at 1, 3, 6, 12, 18, and 24 months after the procedure including 7-day Holter monitoring. Additional telephone interviews were conducted regularly. In case of symptoms suggestive of recurrent arrhythmia, additional visits were immediately initiated.

Endpoints

The primary endpoint was arrhythmia recurrence, defined as a documented episode of AF or atrial tachycardia >30 s irrespective of accompanying symptoms on Holter-ECG or 12-lead ECG. Secondary endpoints were freedom from any atrial arrhythmia at 12 and 24 months after the procedure and any procedure-related complications, such as pericardial effusion, pericardial tamponade, phrenic nerve palsy (PNP), cerebral or peripheral embolism, or atrioesophageal fistula.

Results

Patient characteristics

A total of 40 patients (23 female, 58%) with a mean age of 78.3 ± 2.7 years (median: 78 years, range: 75–87 years) presenting with symptomatic AF (31 (77.5%) pAF, 9 (22.5%) perAF) were included. All patients remained symptomatic with a mean European Heart Rhythm Association (EHRA) score of 2.5 ± 0.5 after rate-control therapy and were either unsuccessfully treated or intolerant to at least one class I or class III antiarrhythmic drug. All patients were treated with the 28-mm second-generation cryoballoon (Arctic Front Advance) as index procedure.

At least 1 electrical cardioversion with recurrence of AF had been performed in all 9 patients suffering from perAF before they were considered for ablation. At baseline, mean $CHADS_2$ score was 3.0 ± 1.1 (range: 1–6) and mean CHA_2DS_2-VASc score was 4.7 ± 1.3 (range: 2–7). 36 patients (90%) had arterial hypertension, 18 patients (45%) had stable coronary artery disease, and 14 patients (35%) had been diagnosed with diabetes mellitus. By echocardiography, left ventricular hypertrophy was found in 15 (38%) patients and clinical heart failure (NYHA II/III) in 9 (23%) patients. Mean LA diameter was 46 ± 6 mm; 37 patients (93%) were on oral anticoagulation therapy at baseline. Detailed baseline characteristics are shown in Table 1.

Procedural data and acute ablation results

At the beginning of the index procedure, 30 of the 40 patients (75.0%) were in sinus rhythm, 9 patients (22.5%) presented in AF, and 1 patient (2.5%) had atrial tachycardia at the beginning of the procedure. In the 40 patients included in the study, we identified a total number of 157 pulmonary veins. Four patients had a left

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