International Journal of Cardiology 176 (2014) 645–650

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Long-term comparison of cryoballoon and radiofrequency ablation of paroxysmal atrial fibrillation: A propensity score matched analysis

Sven Knecht [a,e,1], Christian Sticherling [a,e,1], Stefanie von Felten [b], David Conen [c,e], Beat Schaer [a,e], Peter Ammann [d], David Altmann [d], Stefan Osswald [a,e], Michael Kühne [a,e,*]

[a] Department of Cardiology, University Hospital Basel, Basel, Switzerland
[b] Clinical Trial Unit, University Hospital Basel, Switzerland
[c] Department of Internal Medicine, University Hospital Basel, Switzerland
[d] Department of Cardiology, Kantonsspital St. Gallen, St. Gallen, Switzerland
[e] Cardiovascular Research Institute Basel, University Hospital Basel, Switzerland

ARTICLE INFO

Article history:
Received 13 February 2014
Received in revised form 23 May 2014
Accepted 24 June 2014
Available online 2 July 2014

Keywords:
Atrial fibrillation
Pulmonary vein isolation
Ablation
Cryoballoon
Radiofrequency

ABSTRACT

Background: Although radiofrequency (RF) and cryoballoon (CB) based technologies for pulmonary vein isolation (PVI) have both individually been demonstrated to be effective and safe for the treatment of paroxysmal AF, head-to-head comparisons are lacking. The purpose of this study was to compare the outcome of cryoballoon versus radiofrequency ablation in patients with paroxysmal atrial fibrillation undergoing pulmonary vein isolation.
Methods: Out of a prospective registry of 327 patients undergoing PVI, 208 patients (age 58 ± 11 years, ejection fraction 59 ± 6%, left atrial size 39 ± 6 mm) with paroxysmal AF were identified. The presented dataset was obtained by 1:1 propensity score matching and contained 142 patients undergoing CB-PVI or RF-PVI in conjunction with a 3D mapping system, respectively. We compared single procedure efficacy of the two methods using a Cox proportional hazards model.
Results: After a mean follow-up of 28 months and a single procedure, AF recurred in 37 of 71 (52%) in the CB-PVI group and in 31 of 71 patients (44%) in the RF-PVI group (HR [95% CI] = 1.19 [0.74, 1.92], p = 0.48). Recurrence of AF for PVI using solely the CB was observed in 23 of 51 (45%) patients and in 23 of 51 (45%) patients in the corresponding RF-PVI group (HR [95% CI] = 0.93 [0.52, 1.66], p = 0.81). Complication rate was not different between the groups.
Conclusion: A propensity score matched comparison between CB-PVI and RF-PVI using a 3D-mapping system for AF ablation showed similar long-term success rates.

1. Introduction

Pulmonary vein isolation (PVI) has become the cornerstone of interventional treatment of paroxysmal atrial fibrillation (AF) [1]. Currently, the procedural endpoint of PVI is most frequently achieved by performing point-by-point ablation by means of radiofrequency (RF) energy in combination with an electroanatomical mapping system [2]. A balloon-based technology using cryoenergy for PVI is increasingly used and has been developed in order to simplify the creation of a complete circumferential lesion around the pulmonary veins (PV) with only a limited number of applications [3]. Recently, the safety and efficacy of cryoballoon pulmonary vein isolation (CB-PVI) compared to antiarrhythmic drugs have been shown for the treatment of patients with paroxysmal AF [4] and a plethora of non-randomized single-center studies reporting success rates of CB-PVI have been published [5–11]. In the absence of a randomized trial, we used propensity-score matching to perform an unbiased comparison with long-term follow-up after CB-PVI and RF-PVI in conjunction with an electroanatomical mapping system in patients with paroxysmal AF.

2. Methods

2.1. Study population

We included 327 consecutive patients with documented episodes of AF into the prospective "Basel Atrial Fibrillation Pulmonary Vein Isolation" (BEAT-AF-PVI) cohort study. For the present study patients with paroxysmal AF undergoing PVI, either using RF or balloon-based cryoablation were analyzed. Persistent or permanent AF, a history of any previous left atrial procedure (surgical or percutaneous) or the use of a magnetic navigation system were exclusion criteria for the purpose of this comparison, resulting in 208 potentially eligible patients.

2.2. Study outcome

The primary outcome measures of the study were: 1) Overall single-procedure efficacy of CB-PVI and RF-PVI ("CB-PVI" versus "RF-PVI") and 2) single-procedure efficacy of the

* Corresponding author at: Department of Cardiology, University Hospital Basel, Petersgraben 4, 4031 Basel, Switzerland. Tel.: +41 61 265 25 25; fax: +41 61 265 45 98.
E-mail address: Michael.Kuehne@usb.ch (M. Kühne).
[1] SK and CS contributed equally to this manuscript.

http://dx.doi.org/10.1016/j.ijcard.2014.06.038
0167-5273/

subset of CB-PVI using the CB alone for PVI compared to RF-PVI ("CB-only" versus "RF-PVI"). Single-procedure efficacy was defined as the time to the first recurrence of AF or any atrial tachycardia. Time to recurrence was calculated as the number of days from the first procedure to recurrence of AF.

Secondary outcome measures were procedure-related complications, procedure duration (defined as vascular access to sheath removal), and fluoroscopy duration.

2.3. Electrophysiological procedure

The study was approved by the local ethics committee and informed consent was obtained from all patients. The presence of intracardiac thrombus was ruled out by transesophageal echocardiography in all patients before the procedure. All patients underwent cardiac magnetic resonance imaging or computed tomography to assess left atrial anatomy prior to the procedure. In patients on vitamin-K antagonists, the treatment was not interrupted for the procedure.

All procedures were performed with patients under conscious sedation using propofol, midazolam, and fentanyl. Double transseptal puncture was performed under fluoroscopic guidance. After transseptal puncture, intravenous heparin was used to maintain an activated clotting time of 350–400 s. The sheaths were continuously flushed with heparinized saline. A 20-pole circumferential mapping catheter (Lasso2515, Biosense Webster, Diamond Bar, USA and Inquiry Optima, St. Jude Medical, St. Paul, USA) was advanced into the left atrium through one of the transseptal sheaths. A diagnostic catheter was positioned in the coronary sinus as a reference and for pacing. The endpoint was the elimination of all PV potentials on the circumferential mapping catheter.

2.4. Cryoballoon ablation

CB-PVI was performed as published elsewhere [12]. In order to obtain long-term follow-up as recommended by the HRS/EHRA/ECAS consensus statement [1], the enrollment period for this study ended before the second generation CB became available and only patients undergoing CB-PVI using the first generation CB were analyzed.

A steerable sheath (FlexCath, Medtronic, Minneapolis, USA) was advanced through the second transseptal puncture. The guidewire and the steerable sheath were used to position the CB (Arctic Front, Medtronic, Minneapolis, USA). The use of the 23-mm CB was allowed in patients with a small PV (<20 mm). Orientation of the CB was assessed during contrast injection. A freezing cycle with a standard duration of 300 s was started after PV occlusion was demonstrated by contrast injection. If ablation using the CB alone ("CB-only") was not effective in isolating the PV after up to a maximum of 4 applications, PVI was completed using an irrigated-tip radiofrequency ablation catheter ("CB with RFA" group). A minimum of two freezing cycles per vein was required, including one extra freeze after PVI. Confirmation of PVI was performed using the circumferential mapping catheter in all patients.

2.5. Radiofrequency ablation

RF-PVI was performed using a 3D-mapping system and a 3.5 mm open irrigated-tip catheter. The geometrical reconstruction of the left atrium of the mapping system and the imported reconstruction from magnetic resonance imaging or computed tomography were used to the guide the continuous circumferential antral ablation around the ipsilateral PVs. RF energy was delivered in unipolar mode using the EP Shuttle RF generator (Biosense Webster, Diamond Bar, USA) with power of up to 35 W and a maximum temperature of 50 °C. Power at the posterior wall was limited to 25 W.

2.6. Complications

Peri-interventional and in-hospital complications were included according to the HRS/EHAR/ECAS expert consensus statement on AF ablation if resulting in permanent injury or death, requiring intervention for treatment or prolonging hospitalization for more than 48 h [1]. It includes death, cardiac tamponade and pericardial effusion requiring drainage, stroke or transient ischemic attack, myocardial infarction, atrio-esophageal fistula, any complication requiring heart surgery, and symptomatic persistent phrenic nerve palsy and vascular complications such as atrioventricular fistula, pseudoaneurysm or hematoma requiring surgery. Furthermore, transient phrenic nerve palsy resolving during hospital stay was included.

2.7. Follow-up

All antiarrhythmic drugs were discontinued immediately after the procedure. Follow-up consisted of outpatient clinic visits at 3, 6 and 12 months and then every 12 months after the first and after any repeat procedure and included a detailed history, physical examination, 12-lead ECG, 24-h Holter monitoring and a 7 day Holter at 12 months. Episodes of AF (>30 s) or any sustained left atrial tachycardia were counted as recurrences. A blanking period of 3 months was applied. Patients with recurrent symptomatic AF after the blanking period were offered a repeat procedure.

2.8. Statistical analysis

208 of 327 patients in the registry had paroxysmal AF. For these, all baseline information required for matching (71 with CB-PVI, 137 with RF-PVI) was available. We used baseline information on age, sex, body mass index, diabetes, hypertension, hypercholesterolemia, smoking or history of smoking, documented coronary artery disease, left ventricular ejection fraction and LA size to calculate a propensity score for treatment with CB-PVI. We then performed a 1:1 matching of the CB-PVI patients and patients undergoing RF-PVI, using nearest neighbor matching on the linear propensity score with a maximum caliper width of 0.2 standard deviations. A Cox proportional-hazard model, with PVI as the explanatory variable, was employed to compare CB-PVI with RF-PVI with regard to time to first recurrence of AF for the 1:1-matched dataset (matched analysis). Furthermore, a crude comparison was performed to include the full data set of 208 patients with the same model (unmatched analysis). In addition, Kaplan–Meier curves were drawn to graphically display the data. Baseline characteristics of patients are shown as the number and percentage affected for categorical variables and as the mean ± one standard deviation in combination with the median for continuous variables. The p values were calculated using a Chi^2 test for categorical and a Mann–Whitney test for continuous variables. A p value of <0.05 was considered significant. Statistical analysis was conducted using R (version 3.0.2). The R-package "nonrandom" was used for propensity score estimation and matching [13].

3. Results

3.1. Study population

The resulting propensity score matched data set included 142 patients, 71 with CB-PVI and 71 with RF-PVI. The flowchart of the study with the analyzed groups can be found in Fig. 1. A summary of the baseline characteristics is shown in Table 1. The patients had a mean age of 58 ± 11 years, 74% were men and the left atrial size in the parasternal long axis was 39 ± 6 mm. Atypical PV anatomy was identified in 23 patients (16.3%), with 13 patients (9.2%) having an additional right middle PV, 1 patient an additional right posterior PV (0.7%) and 14 patients (6.3%) a left common ostium. Mean duration of documented AF was 62 ± 70 months and was not significantly different between the groups. Overall mean follow-up of the entire matched patient dataset was 28 ± 15 months.

3.2. Procedural characteristics

3.2.1. Cryoballoon ablation

In 68 of the 71 matched patients, CB-PVI was performed using the 28-mm balloon and in 3 using the 23-mm CB. Acute isolation of all PVs with the CB alone ("CB-only" group) was achieved in 48 of 68 patients (71%) with the 28-mm CB and in all 3 patients (100%) using the 23-mm CB, resulting in an overall CB-only success rate per patient of 72% (51 of 71 patients). The procedural endpoint of PVI in the remaining 20 patients ("CB with RFA" group) was reached in combination with "touch-up" ablation using an irrigated-tip radiofrequency ablation

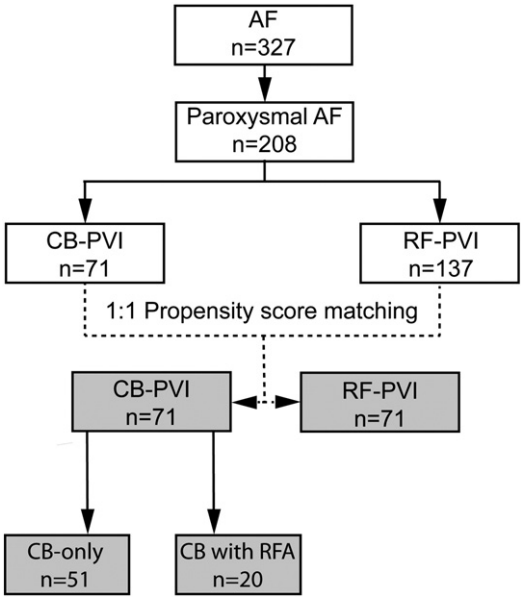

Fig. 1. Flowchart of the patient assignment.