Combined use of cryoballoon and focal open-irrigation radiofrequency ablation for treatment of persistent atrial fibrillation: Results from a pilot study

Moussa Mansour, MD,*† Giovanni B. Forleo, MD, PhD,† Augusto Pappalardo, MD,† Conor Barrett, MD,* E. Kevin Heist, MD,* Andrea Avella, MD,† Gianluigi Bencardino, MD,† Antonio Dello Russo, MD, PhD,† Michela Casella, MD, PhD,† Jeremy N. Ruskin, MD,* Claudio Tondo, MD, PhD*†

*From *Massachusetts General Hospital, Heart Center, Boston, Massachusetts, and †Cardiac Arrhythmia and Heart Failure Research Institute, St. Camillo-Forlanini Hospital, Catholic University of Sacred Heart, Rome, Italy.*

BACKGROUND Pulmonary vein isolation (PVI) achieved using a cryoballoon has been shown to be safe and effective. This treatment modality has limited effectiveness for treatment of persistent atrial fibrillation (AF).

OBJECTIVE The purpose of this study was to evaluate a combined approach using a cryoballoon for treatment of PVI and focal radiofrequency (RF) left atrial substrate ablation for treatment of persistent AF.

METHODS Twenty-two consecutive patients with persistent AF were included in the study. PVI initially was performed with a cryoballoon. Left atrial complex fractionated atrial electrograms (CFAEs) then were ablated using an RF catheter. Finally, linear ablations using the RF catheter were performed.

RESULTS Eighty-three PVs, including five with left common ostia, were targeted and isolated (100%). Seventy-seven (94%) of 82 PVs targeted with the cryoballoon were isolated, and 5 (6%) required use of RF energy to complete isolation. A mean of 9.7 ± 2.6 cryoablation applications per patient was needed to achieve PVI. Median time required for cryoablation per vein was 600 seconds, and mean number of balloon applications per vein was 2.5 ± 1.0. In 19 (86%) patients in whom AF persisted after PVI, CFAE areas were ablated using the RF catheter. Two cases of transient phrenic nerve paralysis occurred. After a single procedure and mean follow-up of 6.0 ± 2.9 months, 86.4% of patients were AF-free without antiarrhythmic drugs.

CONCLUSION A combined approach of cryoablation and RF ablation for treatment of persistent AF is feasible and is associated with a favorable short-term outcome.

KEYWORDS Atrial fibrillation; Balloon catheter; Catheter ablation; Cryoablation; Pulmonary vein isolation

ABBREVIATIONS **AF** = atrial fibrillation; **CFAE** = complex fractionated atrial electrogram; **CS** = coronary sinus; **LA** = left atrium; **PV** = pulmonary vein; **PVI** = pulmonary vein isolation; **RF** = radiofrequency

(Heart Rhythm 2010;7:452–458)

Introduction

Catheter ablation has become one of the primary treatments of symptomatic drug-refractory atrial fibrillation (AF).[1] Although ablation techniques vary among centers, there is a general trend favoring pulmonary vein isolation (PVI) alone for treatment of paroxysmal AF[2–5] and PVI with left atrial (LA) substrate modification for treatment of persistent AF.[6,7]

Most ablation procedures currently are being performed with closed- or open-irrigation radiofrequency energy (RF) catheters, which are capable only of focal ablations. However, achieving PVI with focal RF catheters is a lengthy process that is technically challenging and requires a high degree of skill. Balloon and coil platforms, using different energy sources, are being tested as potential alternatives for focal RF catheters, with the hope of providing a safer, faster, and more effective technology.[8–10] Early clinical and preclinical studies have suggested that PVI using cryoenergy is associated with a low risk of endothelial disruption, thrombogenicity, and PV stenosis compared with RF ablation.[11–16] In addition, published studies have suggested that cryothermal balloon ablation for treatment of paroxysmal AF results in a clinical success rate comparable to that of RF ablation.[17–21] However, clinical success of cryoballoon PVI for treatment of paroxysmal AF has not been

Dr. Mansour has served as a consultant for Bard EP, Medtronic, St. Jude Medical, and Biosense Webster. Dr. Heist has received research support from St. Jude Medical. Dr. Ruskin serves as a consultant to Medtronic and Biosense Webster, a Scientific Steering Committee member for CryoCath, and a Clinical Oversight Committee member for CardioFocus, and has served as a speaker at St. Jude Medical and Boston Scientific Fellows' Educational Programs. Dr. Tondo has served as a member of the advisory board of Biosense Webster, and has been as a consultant for, and received lecture fees from, St. Jude Medical. **Address reprint requests and correspondence:** Dr. Claudio Tondo Cardiac Arrhythmia and Heart Failure Research Institute, St. Camillo-Forlanini Hospital, Catholic University of Sacred Heart, Piazza Carlo Forlanini, 1, 00151 Rome, Italy. E-mail address: c.tondo@libero.it. (Received September 24, 2009; accepted December 11, 2009.)

1547-5271/$ -see front matter doi:10.1016/j.hrthm.2009.12.012

achieved in patients with persistent AF. In fact, the clinical success rate in one study was only 39% among patients with persistent AF,[20] likely because of the need for additional atrial substrate modification in this subgroup. Extensive substrate modification using focal cryoablation catheters is technically feasible but is plagued with a prolonged application time and the inability to create "dragging" ablation lesions due to cryocatheter adherence to tissue, which significantly limits the use of these catheters. In this study, we describe a combined ablation approach for treatment of persistent AF using cryoballoon PVI (Arctic Front, CryoCath, Montreal, Quebec, Canada) and RF ablation for LA substrate modification, including targeting residual triggers and drivers of AF outside the PVs.

Methods

Study population

Twenty-two consecutive patients referred to the St. Camillo-Forlanini Hospital (Rome) for catheter ablation of persistent AF were included in the study. All patients had symptomatic persistent AF of more than 6 months' duration and were refractory to one or more antiarrhythmic medications. Exclusion criteria were as follows: age <18 years or >75 years, ejection fraction <30%, LA size >55 mm, inability to consent, and life expectancy <1 year. Persistent AF was defined according to the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines for management of patients with AF.[1]

Clinical characteristics of the study subjects are listed in Table 1. All patients gave written informed consent, and data collection was performed in accordance with institutional ethics guidelines.

Electrophysiologic study

All patients had effective anticoagulation for al least 1 month, followed by subcutaneous low-molecular-weight heparin 2 to 4 days before the procedure. Preprocedural cardiac computed tomographic scanning was performed in all patients. Warfarin was stopped 2 days before ablation. Transesophageal echocardiography was performed within 48 hours before the procedure in all patients to rule out the presence of atrial thrombi. Intraesophageal temperature was monitored continuously using an intraluminal temperature probe. A multipolar mapping catheter was placed into the right atrium and coronary sinus (CS). In addition, an intracardiac echocardiography probe (Acuson, Siemens, Malvern, PA, USA) was placed in the right atrium. Two transseptal punctures were performed, one for the ablation catheter and the other for the multipolar mapping catheter (PentaRay catheter or circular mapping Lasso catheter, Biosense Webster, Diamond Bar, CA, USA). After transseptal puncture, a bolus of 10,000 units heparin was given, followed by intravenous infusion to maintain an activated clotting time of at least 300 seconds. Three-dimensional reconstruction of the LA and PVs was created for all patients using the NavX mapping system (St. Jude Medical, St. Paul, MN, USA). Surface ECGs and multiple intracardiac local electrograms were recorded at a bandpass of 30 to 500 Hz using a computerized electrophysiologic recording system (Bard Electrophysiology, Andover, MA, USA).

Table 1 Baseline characteristics of the study patients (n = 22)

Variable	
Age (years)	56.6 ± 13.6
Male	17 (77.3)
History of AF (months) [median (interquartile range)]	42 (21–67)
Previously ineffective antiarrhythmic drugs	1.8 ± 0.7
Left atrial diameter, long axis (mm)	46.5 ± 4.3
Ejection fraction (%)	50.6 ± 20.3
Follow-up	6.0 ± 2.9
Comorbidity	
Hypertension	12 (60.0)
Lone AF	3 (14.9)
Dilated cardiomyopathy	4 (20)

Values are given as mean ± SD or number (percent) unless otherwise indicated.

AF = atrial fibrillation.

LA mapping and ablation

The procedure was performed in a stepwise manner. At the beginning of the procedure, a complex fractionated atrial electrogram (CFAE) map was acquired using a multielectrode catheter (Lasso or PentaRay) and automated software (NavX). CFAEs were defined as areas with an average cycle length <120 ms over a 4-second span. The ablation procedure consisted of three steps. In the first step, PVI was performed using a cryoballoon (28- or 23-mm diameter; CryoCath). The size of the cryoballoon was determined based on measurements of PV diameters on the previously acquired computed tomographic scan. After PV occlusion by the cryoballoon was documented by intracardiac echocardiography, cryoablation applications to the PVs were performed for 5 minutes (Figure 1). An additional application was performed after the PV was isolated. No more than 15 minutes of total cryoapplications was performed per vein. Before the right superior PV was targeted, a quadripolar catheter was positioned in the superior vena cava for phrenic nerve stimulation during cryoablation. If loss of phrenic nerve capture was noted during ablation, the ablation was terminated immediately. After cryoablation, a circular multielectrode mapping catheter positioned at each PV ostium was used to confirm isolation. In the second step, ablation of CFAE sites in the LA, right atrium, and CS (identified by semi-automated electrogram mapping) was performed using an externally irrigated catheter (ThermoCool Celsius, 3.5 mm, Biosense Webster) if AF was still present or inducible. Ablation sites were identified by acquiring a post-PVI CFAE map. RF power was limited to 25 W when ablation was performed in the posterior LA. Ablation was performed until AF terminated or until all CFAE sites were ablated. The third step involved placing linear lesions on the roof, mitral isthmus, and septum. These