Catheter ablation using the third-generation cryoballoon provides an enhanced ability to assess time to pulmonary vein isolation facilitating the ablation strategy: Short- and long-term results of a multicenter study

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BACKGROUND Limited data exist on cryoablation of atrial fibrillation (Cryo-AF) using the newly available third-generation (Arctic Front Advance-Short Tip [AFA-ST]) cryoballoon.

OBJECTIVE In this multicenter study, we evaluated the safety and efficacy of Cryo-AF using the AFA-ST vs the second-generation (Arctic Front Advance [AFA]) cryoballoon.

METHODS We examined the procedural safety and efficacy and the short- and long-term clinical outcomes associated with a first-time Cryo-AF performed in 355 consecutive patients (254/355 [72%] with paroxysmal AF), using either the AFA-ST (n = 102) or the AFA (n = 253) cryoballoon catheters.

RESULTS Acute isolation was achieved in 99.6% of all pulmonary veins (PVs) (AFA-ST: 100% vs AFA: 99.4%; $P = .920$). Time to pulmonary vein isolation was recorded in 89.2% of PVs using AFA-ST vs 60.2% using AFA ($P < .001$). PVs targeted using AFA-ST required fewer applications (1.6 ± 0.8 vs 1.7 ± 0.8; $P = .023$), whereas there were no differences in the balloon nadir temperature (AFA-ST: −47.0°C ± 7.3°C vs AFA: −47.5°C ± 7.8°C; $P = .120$) or thaw time (AFA-ST: 41 ± 24 seconds vs AFA: 44 ± 28 seconds; $P = .056$). However, AFA-ST was associated with shorter left atrial dwell time (43 ± 5 minutes vs 53 ± 16 minutes; $P < .001$) and procedure time (71 ± 11 minutes vs 89 ± 25 minutes; $P < .001$). Furthermore, Cryo-AF using AFA-ST was completed more frequently by "single-shot" PV ablation (27.4% vs 20.2%; $P = .031$). Persistent phrenic nerve palsy (AFA-ST: 0% vs AFA: 0.8%; $P = .507$) and procedure-related adverse events (AFA-ST: 1.0% vs AFA: 1.6%; $P = .554$) were similar, as was the freedom from recurrent atrial arrhythmias at 10 months of follow-up (AFA-ST: 81.8% vs AFA: 79.9%; $P = .658$).

CONCLUSION Cryo-AF using the AFA-ST cryoballoon offers an enhanced ability to assess time to pulmonary vein isolation, allowing for fewer cryoapplications and shorter left atrial dwell time and procedure time. Consequently, this allowed for procedural completion more frequently using a "single-shot" PV ablation with equivalent safety and efficacy.

KEYWORDS Catheter ablation; Atrial fibrillation; Cryoablation; Cryoballoon; Pulmonary vein isolation

Introduction

Contemporary studies of cryoablation of atrial fibrillation (Cryo-AF) using the second-generation cryoballoon (Arctic Front Advance [AFA] Medtronic, Inc., Minneapolis, MN) have adopted shorter and fewer cryoapplications while still demonstrating acceptable clinical outcomes.[1–3] Although there are presently no uniform guidelines on the optimal Cryo-AF dosing, a greater emphasis has recently been placed on directing this procedure through objective and quantifiable procedural and biophysical markers.[2] Several studies have identified the time to pulmonary vein (PV) isolation (TT-PVI) as an essential indicator of acute and durable PVI.[4–7] Furthermore, this has shown to reduce the requirement for the number of cryoapplications as well as procedural duration and fluoroscopic utilization.[8] However, TT-PVI cannot always be

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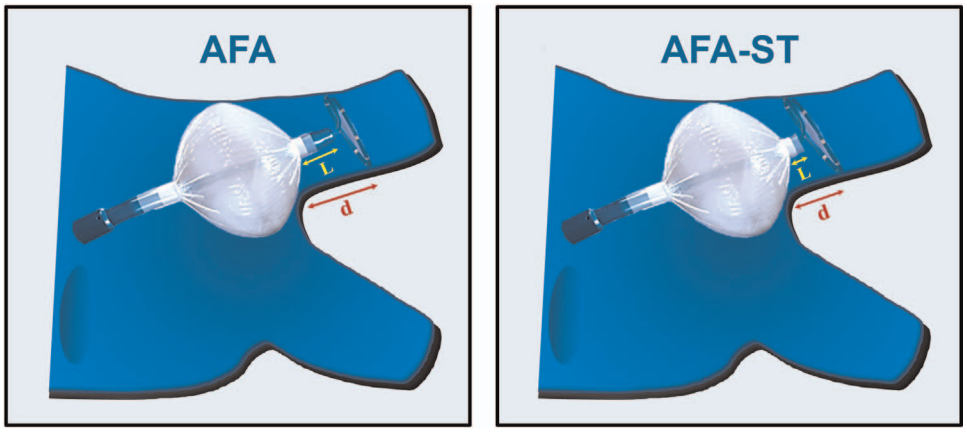

Figure 1 An illustration depicting the principal design change between the AFA and the AFA-ST cryoballoons. As shown, the length of the distal tip (L) of the AFA-ST cryoballoon is ~40% shorter than that of the AFA balloon (8 mm vs 13 mm, respectively), thereby allowing farther withdrawal (d) of the inner lumen circular mapping catheter through the inner lumen of the cryoballoon to a more proximal location within the pulmonary vein ostia. AFA = Arctic Front Advance; AFA-ST = Arctic Front Advance-Short Tip.

measured during Cryo-AF using the AFA cryoballoon.[9] This is at least in part related to the design of this catheter. That is, the AFA catheter's long distal tip can frequently impede sufficient withdrawal of the inner lumen circular mapping catheter (Achieve, Medtronic, Inc.) to a proximal location in the PV ostia where the muscular sleeves typically lie. Consequently, this has led to the development of a third-generation cryoballoon (Arctic Front Advance-Short Tip [AFA-ST], Medtronic, Inc.). Specifically, the 8-mm distal tip of the AFA-ST cryoballoon is ~40% shorter than the 13-mm tip of the AFA. Aside from its significantly shorter distal tip, the design of this novel balloon is overall remarkably similar to that of the AFA catheter (Figure 1). However, there is little data on the safety and efficacy of Cryo-AF using the AFA-ST.

In this multicenter study using a nonrandomized, double-arm, prospective design, we retrospectively analyzed the the short- and long-term outcomes of Cryo-AF using the AFA-ST vs the AFA cryoballoons in a large cohort of patients with symptomatic paroxysmal and persistent atrial fibrillation (AF).

Methods

Study patients

The study cohort consisted of consecutive patients undergoing a first-time Cryo-AF for symptomatic paroxysmal/persistent AF between March 1, 2015 and November 1, 2015. The procedures were performed by 6 experienced operators at 5 centers. The study sites included Mercy General Hospital (Sacramento, CA), Staten Island University Hospital (Staten Island, NY), Jersey Shore University Medical Center (Neptune, NJ), Westside Regional Medical Center (Plantation, FL), and Broward Health Medical Center (Fort Lauderdale, FL). Approval for this study was granted by each facility's institutional review board.

Procedural details

Briefly, diagnostic electrophysiology catheters including a coronary sinus decapolar and a right atrial quadripolar catheter were positioned for recording and pacing, followed by single transseptal catheterization. Intravenous heparin was administered at the time of transseptal puncture followed by an infusion (target activated clotting time ≥300 seconds). All patients underwent PVI using a 23-mm or a 28-mm AFA or AFA-ST cryoballoon catheter inserted through a 12-F steerable sheath (FlexCath, Medtronic, Inc.) over a 20-mm inner lumen circular mapping (Achieve) catheter. In the first phase of the study, all procedures were performed using the AFA balloon. During the second phase, once the AFA-ST balloon became commercially available, all the procedures were then completed using the AFA-ST balloon. Balloon size selection was guided by PV size/anatomy as determined by preprocedural computed tomographic angiography, intraprocedural left atrial (LA) angiography, or intraprocedural intracardiac echocardiography. Optimal cryoballoon positioning was confirmed by PV angiography. All operators followed the same protocol for cryoablation. Attempts were made to specifically record TT-PVI during ablation of each PV, during each and every procedure. Based on the currently available data, either 1 or 2 effective cryoapplications were delivered to each PV, guided by TT-PVI. That is, a single cryoapplication was delivered to a PV if TT-PVI measured ≤60 seconds, whereas a second cryoapplication was delivered if TT-PVI >60 seconds or simply could not be measured. Those cryoapplications that did not achieve a TT-PVI of ≤90 seconds were abandoned. PVI was confirmed by testing for entrance/exit block and after the administration of intravenous adenosine. Luminal esophageal temperature was monitored throughout ablation. Esophageal temperatures <15°C were avoided. During cryoablation of the right PVs, high-output right phrenic nerve (PN) stimulation (10–25 mA; 1000–1200 ms) was performed using the diagnostic quadripolar catheter from within the superior vena cava. Whenever diminished or loss of pacing capture was observed, cryoablation was immediately terminated. PN palsy was classified as either transient or persistent. *Transient PN palsy* was defined as diminished/absence

Table 1 Baseline patient demographics and characteristics

Characteristic	AFA (n = 253)	AFA-ST (n = 102)	*P*
Age (y)	64 ± 10	64 ± 11	.745
Sex: male	172 (68)	71 (70)	.778
Body mass index (kg/m^2)	30 ± 6	31 ± 6	.253
Hypertension	174 (69)	68 (67)	.783
Diabetes mellitus	55 (22)	27 (26)	.505
Dyslipidemia	139 (55)	61 (60)	.449
Sleep apnea	70 (28)	35 (34)	.288
Stroke/transient ischemic attack	26 (10)	16 (16)	.221
LA diameter (mm)	43 ± 6	45 ± 6	.179
LA volume index (mL/m^2)	39 ± 14	43 ± 10	.170
Left ventricular ejection fraction (%)	55 ± 10	56 ± 8	.198
Coronary artery disease	50 (20)	24 (24)	.386
Myocardial infarction	27 (11)	2 (2)	.002*
Percutaneous coronary intervention	34 (13)	10 (10)	.366
Coronary artery bypass graft	22 (9)	14 (14)	.075
Cardiac implantable electronic device	37 (15)	15 (15)	.983
Paroxysmal AF	179 (71)	75 (74)	.663
Prior cardioversion	173 (68)	80 (78)	.071
No. of prior cardioversions per patient	1.0 ± 1.0	1.0 ± 0.8	.551
$CHADS_2$ score	1.4 ± 1.0	1.7 ± 1.2	.113
No. of antiarrhythmic drugs per patient	1.2 ± 0.7	1.3 ± 0.7	.285
Antiplatelet therapy	23 (9)	5 (5)	.139
Oral anticoagulation therapy	218 (86)	86 (84)	.661
Vitamin K antagonist	38 (15)	10 (10)	.173
Novel agent	180 (71)	76 (75)	.565

Values are presented as mean ± SD or as n (%).

AF = atrial fibrillation; AFA = Arctic Front Advance; AFA-ST = Arctic Front Advance-Short Tip; $CHADS_2$ = congestive heart failure, hypertension, age ≥75 y, diabetes, and stroke; LA = left atrial.

*Significant *P* value.

of pacing capture during PN stimulation at the time of ablation with eventual resolution before the end of procedure, whereas persistent PN palsy was characterized by continued loss of PN function that persisted during follow-up. If PN palsy was encountered, the application was terminated and no further ablation was performed using the cryoballoon.

Whenever the PVs could not be completely isolated using cryoablation, point-by-point radiofrequency (RF) ablation was used to achieve this acute end point. Furthermore, arrhythmias other than AF (such as atrial flutter/tachycardia) were targeted using RF ablation. RF ablation was performed using an externally irrigated ablation catheter (ThermoCool SmartTouch, Biosense Webster, Inc., Diamond Bar, CA, or FlexAbility, St. Jude Medical, Inc., St. Paul, MN), guided by 3-dimensional electroanatomic mapping (CARTO, Biosense Webster, Inc., or NavX, St. Jude Medical, Inc.).

Postprocedural management

Patients were discharged from the hospital within 1 day of the procedure. Oral anticoagulation was resumed on the evening after the procedure and continued for a minimum of 3 months. Antiarrhythmic therapy was discontinued within 6 weeks of ablation. In addition to routine electrocardiograms obtained during each follow-up visit, 2- to 4-week ambulatory electrocardiographic monitoring was performed at 6 weeks, 3 months, and 6 months. Freedom from recurrent atrial arrhythmias was defined as >30 seconds on any cardiac rhythm recording after a 90-day postablation blanking period. In patients who opted for redo ablation, repeat computed tomographic angiography was performed to exclude PV stenosis. In those with persistent or unexplained pulmonary symptoms (eg, persistent cough or dyspnea), cardiac computed tomographic angiography was also performed. Patients with persistent PN palsy underwent outpatient serial chest x-ray imaging for reassessment during follow-up.

Statistical methods

Data are expressed as number (percentage) or mean ± SD. Baseline patient demographic characteristics and procedural/clinical characteristics were compared between the cohorts. Continuous variables were analyzed using the 2-sample *t* test or Mann-Whitney *U* test for parametric and nonparametric variables, respectively. The χ^2 or Fisher exact test was used for categorical variables. Time to first recurrence of atrial arrhythmias was analyzed using Kaplan-Meier estimates, and overall freedom from atrial arrhythmias was compared between the 2 catheter groups using the log-rank test. Point estimate comparisons at 10 months postindex ablation were evaluated using a 2-sided *Z* test for difference. For all analyses, *P* values were 2-sided and a $P < .05$ was considered statistically significant. The analyses were conducted with use of Stata 14 (StataCorp LP, College Station, TX), SAS version 9.4 (SAS Institute, Inc.,

Cary, NC), and R statistical package version 3.2.2 (www.r-project.org).

Results

Altogether, data from 355 consecutive patients (72% with paroxysmal AF) who underwent a first-time Cryo-AF using the AFA-ST (n = 102) and the AFA (n = 253) cryoballoons were analyzed. Baseline patient demographic characteristics were similar (Table 1). In total, 407 PVs (4.0 ± 0.3 PVs per patient) were targeted using the AFA-ST and 1009 PVs (4.0 ± 0.3 PVs per patient) using the AFA cryoballoon. The 28-mm cryoballoon was used in nearly all cases (99.7%) (Table 2). Acute isolation was achieved in 99.6% of all PVs, and its frequency was similar between the AFA-ST and the AFA cryoballoons (100% vs 99.4%; $P = .920$). As such, RF ablation was required to complete isolation of 6 of 1009 PVs (0.6%) in 4 of 253 patients (1.6%) using AFA, but none using AFA-ST. TT-PVI was recorded in 89.2% of PVs using AFA-ST as compared with only 60.2% using AFA ($P < .001$). As a result, PVs isolated using AFA-ST required fewer total and effective cryoapplications, but were associated with a higher rate of abandoned cryoapplications (applications unable to achieve optimal TT-PVI as defined by this study's prespecified protocol) (Table 2). AFA-ST was also accompanied by shorter LA dwell time and total procedure time, but with similar fluoroscopic utilization. Furthermore, in 28 patients (27.4%) ablated using AFA-ST, the procedure was successfully completed by "single-shot" PV ablation (single cryoapplication per PV in all the PVs) as opposed to 51 patients (20.2%) targeted using AFA ($P = .031$). In addition, the frequency of recording TT-PVI in a single PV per patient (97% vs 83%; $P < .001$), in 2 PVs per patient (88% vs 62%; $P < .001$), and in 3 PVs per patient (64% vs 40%; $P < .001$) was greater using AFA-ST than using AFA (Figure 2). While there was a trend toward improved recording of TT-PVI in all PVs per patient (34% vs 25%; $P = .072$), this did not reach statistical significance.

Conversely, there were no discernible differences in the duration of TT-PVI, the duration of cryoapplications, balloon nadir temperature, or balloon thaw times between the 2 cryoballoons (Table 2). Moreover, total cryoablation time was similar between the 2 groups, as was the incidence of atrial flutters/tachycardias requiring RF ablation as well as RF duration. PN palsy and procedure-related adverse events were similar between the 2 groups. Furthermore, all patients with transient/persistent PN palsy exhibited complete PVI. The incidences of cardiac tamponade, stroke, atrioesophageal fistula, and death were zero during follow-up. Details about procedural and biophysical variables associated with AFA and AFA-ST cryoballoons by PV type are given in Table 3.

The mean follow-up period in this study was 12 ± 2 months, including 10 ± 1 months for AFA-ST and 13 ± 2 months for AFA. As illustrated in Figure 3, freedom from recurrent atrial arrhythmias did not differ when compared using the log-rank test ($P = .624$). Furthermore, a 2-sided Z test for differences at 10 months postindex ablation demonstrated no statistical difference between the cohorts

Table 2 Procedural characteristics and adverse events

Characteristic or outcome	AFA (n = 253)	AFA-ST (n = 102)	P
Cryoballoon used			
23-mm	1 (0.4)	0 (0.0)	.713
28-mm	252 (99.6)	102 (100.0)	.713
PVs isolated	1003 (99.4)	407 (100.0)	.920
Ablation variables			
TT-PVI (s)	47 ± 16	48 ± 17	.196
Total number of cryoapplications per PV	1.7 ± 0.8	1.6 ± 0.8	.023*
No. of effective cryoapplications per PV	1.5 ± 0.3	1.3 ± 0.3	.034*
No. of abandoned cryoapplications per PV	0.2 ± 0.1	0.3 ± 0.1	.034*
Cryoapplication duration (s)	149 ± 34	150 ± 35	.382
Balloon nadir temperature (°C)	−47.5 ± 7.8	−47.0 ± 7.3	.120
Balloon thaw time (s)	44 ± 28	41 ± 24	.056
Total cryoablation time (min)	17 ± 5	16 ± 4	.224
RF ablation of atrial flutter/tachycardia	36 (14)	17 (17)	.140
Total RF ablation time (min)	10 ± 7	10 ± 11	.710
Procedural variables			
LA dwell time (min)	53 ± 16	43 ± 5	<.001*
Fluoroscopy time (min)	13 ± 5	12 ± 6	.236
Total procedure time (min)	89 ± 25	71 ± 11	<.001*
PN palsy			
Transient	7 (2.8)	2 (2.0)	.736
Persistent	2 (0.8)	0 (0.0)	.507
Other adverse events	4 (1.6)	1 (1.0)	.554
Groin complication	3 (1.2)	0 (0.0)	.361
Pericardial effusion	1 (0.4)	1 (1.0)	.493

Values are presented as mean ± SD or as n (%).

AFA = Arctic Front Advance; AFA-ST = Arctic Front Advance-Short Tip; LA = left atrial; PN = phrenic nerve; PV = pulmonary vein; RF = radiofrequency; TT-PVI = time to pulmonary vein isolation.

*Significant P value.

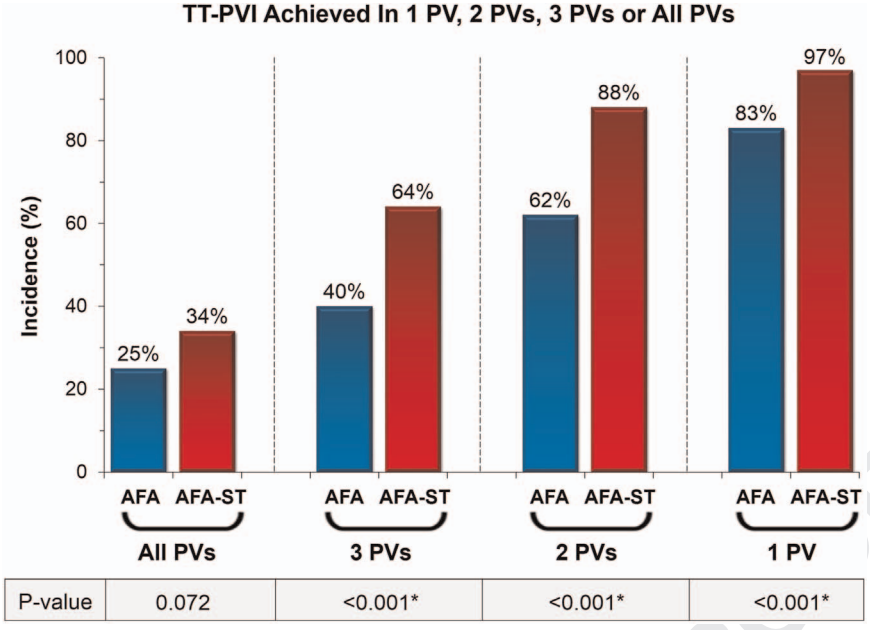

Figure 2 Assessment of TT-PVI by the number of PVs per patient. The frequency of recording TT-PVI in 1 PV per patient (97% vs 83%; $P < .001$), in 2 PVs per patient (88% vs 62%; $P < .001$), and in 3 PVs per patient (64% vs 40%; $P < .001$) was greater using AFA-ST versus AFA. While there was a trend toward improved recording of TT-PVI in all PVs per patient (34% vs 25%; $P = .072$), this did not reach statistical significance. AFA = Arctic Front Advance; AFA-ST = Arctic Front Advance-Short Tip; PV = pulmonary vein; TT-PVI = time to pulmonary vein isolation.

Table 3 Comparisons of procedural and biophysical variables by PV type between the 2 groups

Variable	AFA (n = 1009)	AFA-ST (n = 407)	*P*
Left common PV	19/20 (95.0)	5/5 (100.0)	.627
Cryoapplication duration (s)	157 ± 38	153 ± 36	.782
TT-PVI (s)	56 ± 25	61 ± 7	.797
Nadir balloon temperature (°C)	−41 ± 8	−40 ± 6	.832
Balloon thaw time (s)	18 ± 7	18 ± 6	.785
Left superior PV	233/233 (100.0)	97/97 (100.0)	1.000
Cryoapplication duration (s)	147 ± 34	154 ± 31	.057
TT-PVI (s)	46 ± 17	50 ± 17	.078
Nadir balloon temperature (°C)	−46 ± 8	−46 ± 14	.549
Balloon thaw time (s)	43 ± 25	39 ± 21	.227
Left inferior PV	232/233 (99.6)	97/97 (100.0)	.521
Cryoapplication duration (s)	151 ± 32	156 ± 31	.176
TT-PVI (s)	49 ± 14	51 ± 16	.208
Nadir balloon temperature (°C)	−49 ± 8	−48 ± 8	.062
Balloon thaw time (s)	53 ± 32	48 ± 28	.238
Right superior PV	253/253 (100.0)	102/102 (100.0)	1.000
Cryoapplication duration (s)	150 ± 31	151 ± 32	.826
TT-PVI (s)	45 ± 15	46 ± 15	.569
Nadir balloon temperature (°C)	−48 ± 8	−48 ± 7	.644
Balloon thaw time (s)	46 ± 27	43 ± 26	.526
Right middle PV	17/17 (100.0)	4/4 (100.0)	1.000
Cryoapplication duration (s)	145 ± 33	167 ± 19	.172
TT-PVI (s)	35 ± 19	36 ± 19	.923
Nadir balloon temperature (°C)	−44 ± 8	−51 ± 9	.145
Balloon thaw time (s)	22 ± 18	45 ± 18	.053
Right inferior PV	249/253 (98.4)	102/102 (100.0)	.195
Cryoapplication duration (s)	150 ± 32	153 ± 32	.487
TT-PVI (s)	49 ± 16	52 ± 18	.168
Nadir balloon temperature (°C)	−46 ± 8	−46 ± 7	.970
Balloon thaw time (s)	38 ± 26	33 ± 23	.172

Values are presented as mean ± SD or as n/N (%).

AFA = Arctic Front Advance; AFA-ST = Arctic Front Advance-Short Tip; PV = pulmonary vein; TT-PVI = time to pulmonary vein isolation.

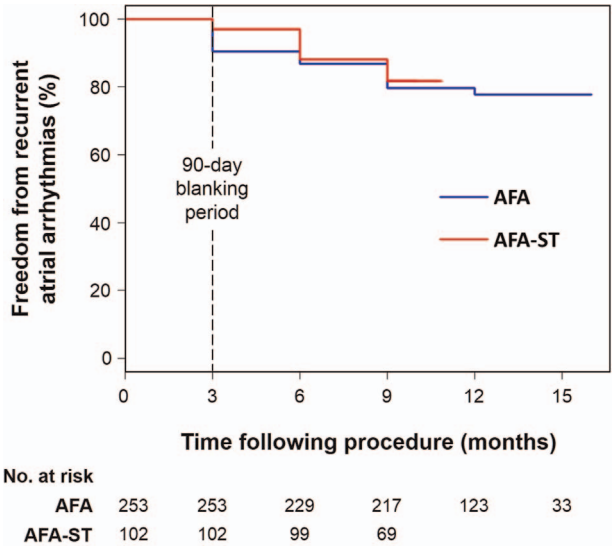

Figure 3 Cumulative freedom from recurrent atrial arrhythmias after cryoballoon ablation of atrial fibrillation. A Kaplan-Meier curve illustrating the cumulative freedom from recurrent atrial arrhythmias after cryoablation using the AFA vs the AFA-ST cryoballoons, including the number of patients at risk. AFA = Arctic Front Advance; AFA-ST = Arctic Front Advance-Short Tip.

(AFA-ST: 81.8% freedom from atrial arrhythmias [95% CI 73.9–89.7] vs AFA: 79.9% freedom from atrial arrhythmias [95% CI 74.7–84.7]; $P = .658$).

In order to evaluate for any potential "learning curve" influences on the data sets, the AFA and AFA-ST cohorts were reexamined after dividing each group into 2 equal halves on the basis of the procedure timelines. When comparing the initial (first-half) phase with the latter (second-half) phase of the AFA cohort, fluoroscopy duration (13 ± 5 minutes vs 13 ± 6 minutes; $P = .639$), LA dwell time (54 ± 12 minutes vs 52 ± 18 minutes LA; $P = .360$), and "single-shot" PV ablation (15.1% vs 25.4%; $P = .060$) did not significantly differ. Only procedure time was shorter during the latter phase in the AFA arm (92 ± 26 minutes vs 85 ± 23 minutes; $P = .021$). Similarly, in the AFA-ST arm, when comparing the initial phase with the latter phase of the study, procedure time (70 ± 12 minutes vs 72 ± 12 minutes; $P = .303$), LA dwell time (43 ± 5 minutes vs 43 ± 5 minutes; $P = .796$), and "single-shot" PV ablation (35.3% vs 19.6%; $P = .120$) did not statistically differ. However, fluoroscopic utilization was slightly longer in the AFA-ST arm during the latter phase of the study (11 ± 5 minutes vs 14 ± 7 minutes; $P = .034$).

Four patients (3.9%) ablated using AFA-ST and 18 patients (7.1%) ablated using AFA underwent a redo procedure because of recurrent symptomatic atrial arrhythmias, and all were deemed as clinical efficacy failures in this study analysis. In 3 patients treated with AFA-ST (75%), all PVs were found to be electrically isolated during the redo procedure. One patient exhibited reconnection of the right inferior PV, which was reablated. In the AFA arm, 15 of 18 patients (83%) exhibited durable isolation of all PVs during the redo procedure. The remaining 3 patients each exhibited single PV reconnection, which were also reisolated. Of these, 2 patients had developed reconnection of the right inferior PV, and 1 patient exhibited reconnection of the left inferior PV.

Discussion

This analysis represents the first, large multicenter report on the short- and long-term safety and efficacy outcomes of Cryo-AF using the novel third-generation AFA-ST cryoballoon. As such, it provides several pertinent insights. First, it shows that TT-PVI during Cryo-AF can be recorded more readily using AFA-ST as compared with its second-generation predecessor. Consequently, effective PVI using AFA-ST was consistently attained by means of fewer cryoapplications. Second, AFA-ST allowed more frequent procedural completion through "single-shot" PV ablation, without compromising clinical efficacy. Third, both LA dwell time and total procedure time were considerably reduced. Lastly, freedom from recurrent atrial arrhythmias was similar between the 2 balloons during long-term follow-up.

Cryo-AF has emerged as a practical and effective strategy for the treatment of AF.[10] Nonetheless, the optimal cryoablation dosing still remains unclear. Several studies have established the utility of monitoring TT-PVI using an inner lumen circular mapping catheter. Chierchia et al[5] illustrated that early PV reconnection was associated with a significantly longer TT-PVI (117 ± 25 seconds vs 59 ± 25 seconds) as recorded using this approach. Similarly, Chun et al[6] showed that a TT-PVI associated with durable PVI was significantly shorter than in those with electrical reconnection (66 ± 56 seconds vs 129 ± 76 seconds). Kühne et al[7] further corroborated these findings by identifying a mean TT-PVI of 61 seconds in PVs exhibiting permanent isolation as compared with 184 seconds in those with conduction recovery. More recently, a multicenter analysis has established that among the various procedural and biophysical variables of Cryo-AF, a TT-PVI of ≤60 seconds represents the best indicator of durable PVI during long-term follow-up.[4]

Meanwhile, in most studies as well as in clinical practice TT-PVI cannot always be consistently measured. This has in part been a reflection of the design of the AFA cryoballoon. Specifically, the prolonged distal tip of AFA can frequently physically impede sufficient withdrawal of the inner lumen circular mapping catheter to a proximal position within the PV ostia. Since the PV muscular sleeves typically occupy only the proximal segments of the PVs, this catheter design can often hinder the ability to routinely assess TT-PVI.[9] In fact, in most studies the ability to reliably assess TT-PVI using the circular mapping and AFA catheters is reported in only ~50% of the PVs.[5–7,9] However, recent design modifications have led to the development of the AFA-ST balloon that exhibits a much shorter distal tip (Figure 1). Two recent single-center studies[11,12] have demonstrated higher rates of real-time electrical PV recordings using the AFA-ST cryoballoon. As illustrated in the present study, this design adjustment not only enhanced the ability to record PV

electrograms within the PV ostia and TT-PVI in real time but also improved the procedural efficiency by minimizing the number of total and effective cryoapplications, LA dwell time, and total procedure time. In essence, AFA-ST enhanced the frequency of "electrogram-guided" vs "empiric" cryoapplications. Ultimately, this translated into a higher rate of procedural completion by "single-shot" PV ablation while still maintaining clinical efficacy. In contrast, total cryoablation time was similar when comparing the 2 balloons. That is, the time gained from fewer effective cryoapplications needed to achieve PVI using AFA-ST was partially offset by a higher incidence of abandoned cryoapplications needed to optimally achieve this end point. As such, AFA-ST maximized the delivery of effective cryoapplications, whereas ablation using AFA depended to a greater extent on "empiric" ablation and driven less by PV electrograms or PVI. Moreover, the biophysical characteristics of the AFA-ST catheter appear strikingly similar to those of the AFA balloon.

The improved biophysical properties and superior efficacy associated with the AFA balloon over the first-generation cryoballoon (Arctic Front. Medtronic, Inc.) has been well-described.[13,14] This is thought to be related to the increased number and location of the refrigerant injection ports incorporated into the AFA balloon, which, in turn, results in the expansion of the maximal cooling zone beyond this balloon's equator to the entire distal half of its surface and including the distal tip. Even though there are subtle differences in the internal design of AFA-ST and AFA, it is reassuring to note that the biophysical behaviors of these 2 ablation catheters are essentially similar. Likewise, the adverse event rates including that of PN palsy were equivalent between AFA-ST and AFA balloons. Moreover, in spite of its much shorter distal tip there were no discernible catheter/balloon stability issues concerning the AFA-ST balloon reported by any of the operators in this study. Although in their study, Heeger et al[11] found slightly higher nadir temperatures associated with the AFA-ST balloon (presumably because of a more proximal displacement of the thermocouple on AFA-ST than on AFA), this was not evident in the present study. In fact, we found no significant differences in balloon nadir temperature, duration of TT-PVI, or balloon thaw times associated with the 2 balloon catheters. This is not surprising since the absolute cryoballoon nadir temperature is subject to considerable variation as a consequence of a multitude of dependent and independent variables such as the size of the cryoballoon used (23-mm vs 28-mm, with the latter exhibiting 50% greater surface area), the balloon position within the PV ostia (proximal vs distal), balloon to PV diameter ratio, ipsilateral PV blood flow, and even subtle manipulations by the operator. Thus, as one would expect, balloon nadir temperature by itself has also been shown to serve as only a weak indicator of long-term procedural efficacy and PVI durability.[4]

In summary, the main findings of this analysis suggest that AFA-ST is superior to its second-generation predecessor by providing an improved ability to record PV electrograms and assessing TT-PVI. This was, in turn, accompanied by inherent procedural efficiencies, including fewer total and effective cryoapplications and shorter LA dwell time and total procedure time. Furthermore, it enhanced the ability to complete Cryo-AF using a "single-shot" technique, without compromising safety or procedural and clinical efficacy. However, it needs to be emphasized that although AFA-ST offers an improved ability to assess TT-PVI, this by itself is insufficient to guarantee a successful outcome. As such, the operator must still follow and use the procedural and biophysical indicators necessary to achieve effective PVI.[4]

Study limitations

First, this study represents a large, nonrandomized, double-arm analysis of consecutive patients undergoing Cryo-AF using the AFA or the AFA-ST cryoballoons. As such, since the treatment allocation was nonrandomized, we cannot exclude unknown characteristics that may have confounded either treatment arm. Second, since this was a multicenter study, slight variations in ablation strategy and periprocedural management and monitoring may have existed among operators and centers. Third, subclinical manifestation of certain complications such as esophageal ulceration or PV stenosis could not be excluded, since routine diagnostic studies were not performed to investigate such adverse events. Fourth, the data presented on PV reconnection pertains only to those who underwent repeat ablation and was unavailable for the entire cohort. Fifth, the authors cannot exclude the possibility of temporal bias. That is, in the initial period of the study, all Cryo-AF cases were consecutively performed using the AFA balloon whereas all the cases in the second part of the study were performed using the AFA-ST balloon. Furthermore, recurrent asymptomatic episodes of atrial arrhythmias after Cryo-AF could have occurred without detection during follow-up. However, it would seem unlikely that this would have served as a significant source of bias specifically favoring one or the other treatment arm. Lastly, it should be emphasized that although AFA-ST appears to represent an improved tool for the assessment of TT-PVI, this alone is insufficient to ensure effective PVI. Moreover, the observed benefits associated with AFA-ST were all related to procedural outcomes and not arrhythmia recurrence.

Conclusion

Cryo-AF using the newly available AFA-ST offers an enhanced ability to record TT-PVI as compared with its second-generation predecessor. This allowed for fewer total and effective cryoapplications and shorter LA dwell time and total procedure time. Furthermore, with the use of this novel balloon, Cryo-AF could be completed more frequently by means of "single-shot" PV ablation while maintaining equivalent procedural safety and clinical efficacy.

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