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Paroxysmal AF Catheter Ablation With a Contact Force Sensing Catheter

Results of the Prospective, Multicenter SMART-AF Trial

Andrea Natale, MD,*†‡§‖¶ Vivek Y. Reddy, MD,# George Monir, MD,** David J. Wilber, MD,†† Bruce D. Lindsay, MD,‡‡ H. Thomas McElderry, MD,§§ Charan Kantipudi, MD,‖‖ Moussa C. Mansour, MD,¶¶ Daniel P. Melby, MD,## Douglas L. Packer, MD,*** Hiroshi Nakagawa, MD,††† Baohui Zhang, MS, SM,‡‡‡ Robert B. Stagg, PhD,‡‡‡ Lee Ming Boo, PharmD,‡‡‡ Francis E. Marchlinski, MD§§§

ABSTRACT

BACKGROUND Catheter ablation is important for treatment of paroxysmal atrial fibrillation (PAF). Limited animal and human studies suggest a correlation between electrode-tissue contact and radiofrequency lesion generation.

OBJECTIVES The study sought to assess the safety and effectiveness of an irrigated, contact force (CF)-sensing catheter in the treatment of drug refractory symptomatic PAF.

METHODS A prospective, multicenter, nonrandomized study was conducted. Enrollment criteria included: ≥3 symptomatic episodes of PAF within 6 months of enrollment and failure of ≥1 antiarrhythmic drug (Class I to IV). Ablation included pulmonary vein isolation with confirmed entrance block as procedural endpoint.

RESULTS A total of 172 patients were enrolled at 21 sites, where 161 patients had a study catheter inserted and 160 patients underwent radiofrequency application. Procedural-related serious adverse events occurring within 7 days of the procedure included tamponade (n = 4), pericarditis (n = 3), heart block (n = 1, prior to radiofrequency application), and vascular access complications (n = 4). By Kaplan-Meier analyses, 12-month freedom from atrial fibrillation/atrial flutter/atrial tachycardia recurrence was 72.5%. The average CF per procedure was 17.9 ± 9.4 g. When the CF employed was between investigator selected working ranges ≥80% of the time during therapy, outcomes were 4.25 times more likely to be successful (p = 0.0054; 95% confidence interval: 1.53 to 11.79).

CONCLUSIONS The SMART-AF trial demonstrated that this irrigated CF-sensing catheter is safe and effective for the treatment of drug refractory symptomatic PAF, with no unanticipated device-related adverse events. The increased percent of time within investigator-targeted CF ranges correlates with increased freedom from arrhythmia recurrence. Stable CF during radiofrequency application increases the likelihood of 12-month success. (THERMOCOOL® SMARTTOUCH® Catheter for Treatment of Symptomatic Paroxysmal Atrial Fibrillation; NCT01385202) (J Am Coll Cardiol 2014;64:647-56) © 2014 by the American College of Cardiology Foundation.

From the *Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Austin, Texas; †Division of Cardiology, Stanford University, Stanford, California; ‡Case Western Reserve University, Cleveland, Ohio; §EP Services, California Pacific Medical Center, San Francisco, California; ‖Interventional Electrophysiology, Scripps Clinic, San Diego, California; ¶Department of Biomedical Engineering, University of Texas, Austin, Texas; #Icahn School of Medicine at Mount Sinai, New York, New York; **Florida Hospital Cardiovascular Institute, Orlando, Florida; ††Loyola University, Maywood, Illinois; ‡‡Cleveland Clinic Foundation, Cleveland, Ohio; §§University of Alabama at Birmingham; Birmingham, Alabama; ‖‖Piedmont Heart Institute, Atlanta, Georgia; ¶¶Massachusetts General Hospital, Boston, Massachusetts; ##Minneapolis Heart Institute Foundation, Minneapolis, Minnesota; ***Mayo Clinic, Rochester, Minnesota; †††University of Oklahoma Health Science Center, Oklahoma City, Oklahoma; ‡‡‡Biosense Webster, Inc., Diamond Bar, California; and the §§§Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.
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ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drug
AF = atrial fibrillation
AFL = atrial flutter
AT = atrial tachycardia
CF = contact force
CI = confidence interval
KM = Kaplan-Meier
LA = left atrium/left atrial
PAF = paroxysmal atrial fibrillation
PV = pulmonary vein
QOL = quality of life

Radiofrequency catheter ablation therapy is an important treatment for atrial fibrillation (AF) (1). The cornerstone of AF ablation involves creation of a series of lesions via resistive heating encircling the pulmonary veins (PV), isolating spontaneous ectopic beats from the left atrium (LA) (2). Lesion formation is traditionally monitored as electrogram diminution and impedance drop during application. Missing from this procedure is knowledge of electrode-to-tissue interaction.

Several in vivo and in vitro studies have shown a correlation between electrode-tissue contact and lesion generation (3,4). A recent clinical study using a contact force (CF)-sensing catheter suggested that CF during ablation correlates with clinical outcome in AF patients (5,6).

SEE PAGE 657

The CF catheter used in the present study was developed using a small spring connecting the ablation tip electrode to the catheter shaft with a magnetic transmitter and sensors to measure microdeflection of the spring (7,8). This system has a CF resolution <1 g in bench testing (7,8). SMART-AF was conducted to evaluate the safety and effectiveness of this catheter during standard ablation procedures.

METHODS

The institutional review board or ethics committee at each of the 21 participating centers approved the study protocol (see the Online Appendix for a list of the clinical sites and participating investigators). All patients enrolled in the study provided written informed consent and each site assigned a sequential identification number.

STUDY DESIGN. The prospective, multicenter, nonrandomized clinical study was designed to evaluate the safety and effectiveness of drug-refractory paroxysmal AF (PAF) ablation utilizing the ThermoCool SmartTouch Catheter (Biosense Webster, Inc., Diamond Bar, California) compared to predetermined performance goals. The ablation catheter has been described in detail elsewhere (7,8).

Patients were observed at 1, 3, 6, 9, and 12 months post-ablation, with a 3-month blanking period for anatomical and electrical remodeling of the LA. Electrocardiograms were obtained at all follow-up visits. Transtelephonic monitoring (PER900; Agility Centralized Research Service, Bannockburn, Illinois) was performed during the 9-month post-blanking period. Patients were required to transmit all symptomatic cardiac episodes and to provide additional scheduled transmissions irrespective of symptoms: weekly for the first 8 weeks, then monthly thereafter. An independent safety monitoring committee reviewed and adjudicated all adverse events.

STUDY POPULATION. Enrollment required at least 3 symptomatic AF episodes within the 6 months before enrollment (1 AF episode documented within 1 year), and nonresponse to at least 1 antiarrhythmic drug (AAD) (Class I, Class III, or atrioventricular nodal blocker).

annual royalties >$10,000, the federal threshold for significant financial interest. Dr. Natale has received honoraria/consulting fees from Biosense Webster, Inc., St. Jude Medical, Medtronic, Boston Scientific, Biotronik, and Janssen outside the submitted work. Dr. Reddy has received grants from Biosense Webster, Inc. during the conduct of the study; personal fees from Biosense Webster, Inc. outside the submitted work; and consulting fees from St. Jude Medical. Dr. Monir has received personal fees from Biosense Webster, Inc. outside the submitted work. Dr. Wilber has received grants and lecture/consultant fees from Biosense Webster, Inc.; grants and consultant fees from Medtronic; and lecture fees from St. Jude Medical, outside the submitted work. Dr. Lindsay has received honoraria fees for educational programs and serves on the scientific advisory board from Biosense Webster, Inc., outside the submitted work. Dr. McElderry has received personal fees from Biosense Webster, Inc.; grants and personal fees from Boston Scientific; and personal fees from St. Jude Medical, outside the submitted work. Dr. Mansour has received grant support from St. Jude Medical, Boston Scientific, Biosense Webster, Inc., and MC10 outside the submitted work; and personal fees (consultation fee) from Biosense Webster, Inc. Dr. Packer has provided consulting services for Abiomed, Biosense Webster, Inc., Boston Scientific, CardioDX, CardioFocus, CardioInsight Technologies, Excerpta Medica, FoxP2 Medica LLC, InfoBionic, Inc., Johnson & Johnson Healthcare Systems, Johnson & Johnson, MediaSphere Medical, LLC, Medtronic CryoCath, OrthoMcNeill, Sanofi-Aventis, Siemens, St. Jude Medical, and Siemens AG, and has received no personal compensation for these consulting activities; has received research funding from Biosense Webster, Inc., Boston Scientific/EPT, Endosense, EpiEP, EP Advocate, Medtronic CryoCath LP, Minnesota Partnership for Biotechnology and Medical Genomics/University of Minnesota, National Institutes of Health, CardioFocus, Hansen Medical, Siemens P4D, St. Jude Medical, Siemens AcuNav, and Thermedical (EP Limited); and has received royalties from Blackwell Publishing and St. Jude Medical. Dr. Nakagawa has received grant support from Biosense Webster, Inc. during the conduct of the study as well as grants and personal fees from Biosense Webster, Inc. outside the submitted work. Ms. Zhang and Dr. Boo are employees of Biosense Webster, Inc. Dr. Stagg is an employee of Biosense Webster, Inc. and Johnson & Johnson, and owns stock (<$10,000) in Johnson & Johnson. Dr. Marchlinski has received consultant fees and lecture honoraria from Biosense Webster, Inc.

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Study exclusion criteria were patients <18 years of age, AF of more than 30 days in duration, ejection fraction <40%, previous AF ablation, documented LA thrombus, amiodarone therapy or coronary artery bypass graft procedure in the previous 6 months, New York Heart Association (NYHA) functional class III or class IV, myocardial infarction within the previous 2 months, thromboembolic event in the previous 12 months, severe pulmonary disease, prior valvular cardiac surgical procedure, presence of an implanted cardioverter-defibrillator, contraindication to antiarrhythmic or anticoagulation medications, life expectancy of <12 months, and LA ≥50 mm in the parasternal long axis view.

CATHETER ABLATION. PV isolation with confirmation of entrance block was required (1). Three-dimensional electroanatomical mapping was performed using the Carto 3 System (Biosense Webster, Inc.). Steerable sheath was used in 51.5% of all procedures. CF measurements were sampled at 50 ms (20 Hz) intervals during radiofrequency application. The PVs were isolated by a circumferential lesion set. In the event of spontaneous or induced AF and/or atrial flutter (AFL), additional ablation was allowed at the investigator discretion and included LA linear lesions (roof line between both superior PVs, mitral isthmus line between mitral annulus and left inferior PV, or anterior line between the LA roof and mitral annulus), ablation at sites with electrogram fractionation, and cavotricuspid isthmus ablation. Infusion of isoproterenol (≤20 μg/min) was recommended post-ablation to confirm that all AF foci had been identified, eliminated, or isolated. After the initial procedure, patients were allowed up to 2 repeat ablation procedures within 90 days of the index procedure. At the discretion of the investigator, a previously ineffective drug, at the same dose or lower, could be continued during the effectiveness evaluation period. Following ablation, anticoagulation with warfarin was required for the initial 3 months. Subsequent use of anticoagulation during the effectiveness evaluation period followed current guidelines (9).

ROLL-IN CASES AND CF WORKING RANGES. Each investigator was required to recruit 1 to 2 "calibration roll-in" subjects (at the investigator's discretion), in which investigators would calibrate their individual tactile feel, catheter manipulation technique, and use of other surrogate measures (e.g., electrogram signal, impedance) during the procedure with the displayed CF. During the calibration roll-in procedure(s), the investigators selected the reference ranges based on training. No working range was prescribed.

At the end of the procedure, investigators reviewed offline the CF measured during the roll-in case(s). Investigators were then able to use the information to configure the operating reference ranges for their subsequent cases. The selection of working range could change as investigators performed additional cases in the study.

EFFECTIVENESS OUTCOMES. The effectiveness outcome was freedom from documented symptomatic AF/atrial tachycardia (AT)/AFL during the evaluation period. AF/AT/AFL episodes of ≥30 s were considered recurrent events. Per study protocol, patients with absence of entrance block confirmed in all PVs at the end of the ablation procedure, repeat ablation after Day 90, or changes in specified drug regimen post-blanking also were considered treatment failures, even if the patient remained free from symptomatic AF/AT/AFL.

SAFETY OUTCOMES. Major adverse events were defined as procedure- or device-related serious adverse events (e.g., tamponade, pericarditis, pericardial effusion, perforation), which occurred within 7 days following the ablation procedure, including PV stenosis and atrioesophageal fistula that occurred >7 days post-procedure.

ADDITIONAL OUTCOMES. Additional patient-reported outcomes included assessment of quality of life (QOL) using the 36-item Short Form Health Survey Version 2 (10) and the AF Symptom Frequency and Severity Checklist (11). In addition, the effectiveness outcome of freedom from AF/AT/AFL recurrences post-initial ablation procedures and off Class I/III AAD at 12 months follow-up visit also was analyzed and summarized.

STATISTICAL METHODS. A Kaplan-Meier (KM) curve was plotted for the time to first AF/AT/AFL recurrence following initial ablation procedures. The probabilities of freedom from AF/AT/AFL recurrence at each monthly follow-up time point post-blanking, along with the corresponding 95% confidence intervals (CIs) using Greenwood's formula, were presented. This analysis was stratified by the percentage of time with CF within each investigator's selected ranges dichotomized at its median value of 80%.

The correlations of average CF and percentage of time of CF ≥40 g, dichotomized at the median values, with major adverse events and tamponade were examined. The correlations of average CF and percentage of time of CF with investigator selected ranges, dichotomized at the median value of 80%, with freedom from AF/AFL/AT recurrence were examined. Fisher exact test and logistic regression

analyses were performed to test for significant associations. In the logistic regression analyses, subjects with any major adverse events or tamponade and subjects free from AF/AFL/AT recurrence were treated as outcome and the CF measurements were treated as independent variables. Forward selection method was used to include the potential confounders of demographics, baseline characteristics, and procedural parameters that were associated with the outcome at p value <0.2 at model entry, as well as the clinically meaningful confounders. Only the variables that remained significant at p value <0.05 were included in the final multivariate model in addition to the clinically meaningful confounders.

The statistical significance of change from baseline in QOL measures at each follow-up visit was assessed using a 1-sample Student *t* test compared to no change.

RESULTS

Between June 2, 2011, and December 22, 2011, 172 patients were enrolled in the study. The last follow-up visit in the study occurred on January 31, 2013. Subject disposition and accountability are provided in Figure 1. Of 172 enrolled patients, 161 patients had the investigational catheter inserted and comprised the safety cohort. Radiofrequency ablation was performed on 160 of the patients, and 38 of these patients were "roll-in" patients. The remaining 122 patients comprised the effectiveness cohort, which consisted of enrolled patients who were ablated. Five of 122 effectiveness cohort patients were lost to follow-up before reaching the 12-month follow-up visit. Patient characteristics are described in Table 1.

Average procedure time was 3.7 ± 1.4 h, with an average of 2.0 ± 1.0 h ablation procedure time (from the time of first radiofrequency application to the time of last application). Average fluoroscopy time per procedure was 41.5 ± 26.0 min. Average power applied during radiofrequency application was 31.1 ± 4.1 W.

Per protocol, all index procedures (100.0%, 160 of 160) targeted the PVs. Of these procedures, 50.0% (80 of 160) involved only PV isolation. The remaining procedures (50%) included additional atrial targets: 41.2% only additional linear lesions, 1.9% only focal non-PV targets, and 6.9% linear lesions and focal non-PV targets. Cavotricuspid isthmus ablation was performed in 19.4% (31 of 160) of the index procedures.

Based on the effectiveness cohort, KM analysis shows that the probability of freedom from the per-protocol effectiveness failure at 12 months post-index procedure was 72.5% (95% CI: 64% to 80.5%; transtelephonic compliance = 83.9 ± 17.21%). This

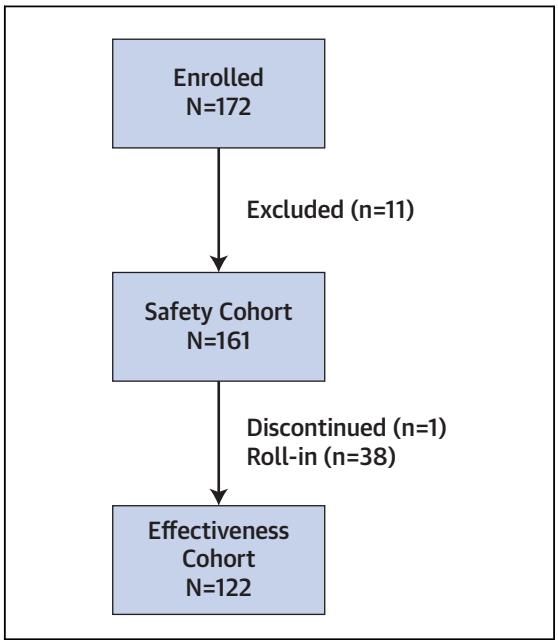

FIGURE 1 Patient Flow Diagram

Disposition of subjects in the study. Excluded patients: enrolled patients who never underwent insertion of the study catheter; discontinued subjects: enrolled patients who had the study catheter inserted but were not ablated; roll-in patients: the first 1 or 2 enrolled patient(s) treated with the study catheter.

includes 2 subjects who were deemed failures because new AADs were administered during the effectiveness evaluation period. One subject had the drug stopped on Day 104, and the second was given a new AAD (a higher dose of metoprolol than the subject previously took) at the 9-month visit. These 2 subjects did not have recurrence after the initial procedure. Because the lower bound of the 95% CI for this KM graph is greater than the 50% pre-determined performance criterion, the per-protocol effectiveness outcome met the performance goal. In addition, based on the effectiveness cohort, there were no statistical differences in per-protocol primary effectiveness between patients who received PV isolation, only as compared to those who received additional linear/foci targets.

For the effectiveness cohort, the probability of freedom from symptomatic and all (symptomatic or asymptomatic) atrial arrhythmia (AF/AFL/AT) recurrence at 12-month follow-up visit were 74.0% (95% CI: 66% to 82%) (Fig. 2) and 69.9% (95% CI: 62% to 78%), respectively. The success rate after a single ablation procedure and off drugs (Class I/III AAD) at 12 months was 65.8% with a lower bound of the 95% CI of 56.5% (Table 2).

The overall average CF recorded during a study ablation procedure for all subjects undergoing ablation (n = 160) was 17.9 ± 9.42 g. Figure 3 presents the histogram distribution of the average CF used during radiofrequency application with average CF shown in 5 g increments. The majority of procedures (efficacy cohort 68.8%, 77 of 112; safety cohort 68.1%, 96 of 141) were completed with average CF between 10 and 25 g.

Based on their roll-in cases and experience as the study progressed, investigators chose working ranges for radiofrequency applications that varied from 4 to 60 g. Working ranges of 5 to 40 g were selected for 67.4% of all study procedures. Figure 4 presents the percentage of time investigators spent in their selected ranges during radiofrequency applications by cohort. Overall, investigators remained in their preselected working CF ranges 73.3 ± 18.35% of the time during radiofrequency application. Most ablation procedures were conducted with the investigators working in their selected ranges 65% to 95% of the time.

Higher average CF during radiofrequency application was not found to correlate with effectiveness. KM analysis using the effectiveness cohort was performed to compare the effectiveness outcome by the investigators' selected working ranges during radiofrequency application ≥80% and <80%. As seen in Figure 5, investigators working in their selected ranges ≥80% of the time during radiofrequency application demonstrated a significant increase of 15% in the effectiveness success at 12 months compared with those working in their selected ranges <80% of the time (81% vs. 66%, respectively; p = 0.0440 [Wilcoxon test]).

Multivariate logistic regression analyses of risk factors for the effectiveness outcome (Table 3) showed that the percentage of time with CF within investigator selected working ranges ≥80% during therapy was significantly associated with positive effectiveness outcomes (p = 0.0054; odds ratio: 4.25; 95% CI: 1.53 to 11.79), and longer procedure time was negatively associated with effectiveness outcome (p = 0.0340; odds ratio: 0.99; 95% CI: 0.99 to 1.00).

Within the safety cohort (n = 161), there were no deaths, stroke, cerebrovascular accident, atrioesophageal fistula, myocardial infarction, thromboembolism, or PV stenosis that occurred within the study period. Procedure-related major adverse events occurring within 7 days of the ablation procedure, as adjudicated by an independent safety committee, included: tamponade (n = 4), pericarditis (n = 3), transient heart block (n = 1, prior to radiofrequency application), and 4 vascular access complications

TABLE 1 Baseline Patient Characteristics

	Effectiveness Cohort (n = 122)	Safety Cohort (n = 161)
Age, yrs	58.3 ± 10.93	58.7 ± 10.83
Male	87 (71.3)	116 (72.0)
Patient history		
AF duration, yrs	4.0 (1.4–7.1)	4.0 (1.5–7.5)
Atrial flutter	37 (30.3)	52 (32.3)
Hypertension	74 (60.7)	96 (59.6)
Diabetes	14 (11.5)	20 (12.4)
Structural heart disease	15 (12.3)	19 (11.8)
Cerebrovascular accident/TIA	0 (0.0)/4 (3.3)	0 (0.0)/5 (3.1)
Prior thromboembolic events	6 (4.9)	10 (6.2)
NYHA functional class		
None	101 (82.8)	133 (82.6)
I	15 (12.3)	18 (11.2)
II	5 (4.1)	8 (5.0)
Unknown	1 (0.8)	2 (1.2)
Failed antiarrhythmic drug class		
I/III at baseline	62 (50.82)	79 (49.07)
II/IV only	17 (13.93)	24 (14.92)
Baseline antiarrhythmic medications		
I/III taking at baseline	78 (63.93)	104 (64.60)
II/IV taking at baseline	59 (48.36)	81 (50.31)
Baseline QOL score		
Mental component summary	49.2 ± 11.2	49.7 ± 11.1
Physical component summary	39.2 ± 7.4	39.1 ± 7.7
Symptom frequency score	20.8 ± 10.3	21.1 ± 10.8
Symptom severity score	16.9 ± 8.7	17.2 ± 8.8
LVEF, mm	60.3 ± 7.8, 40/84	60.2 ± 7.6, 40/84
LA dimension, mm	38.5 ± 5.6, 26/50	38.5 ± 5.7, 21/51

Values are mean ± SD, n (%), median (interquartile range), or minimum/maximum.
LA = left atrium; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; QOL = quality of life; TIA = transient ischemic attack.

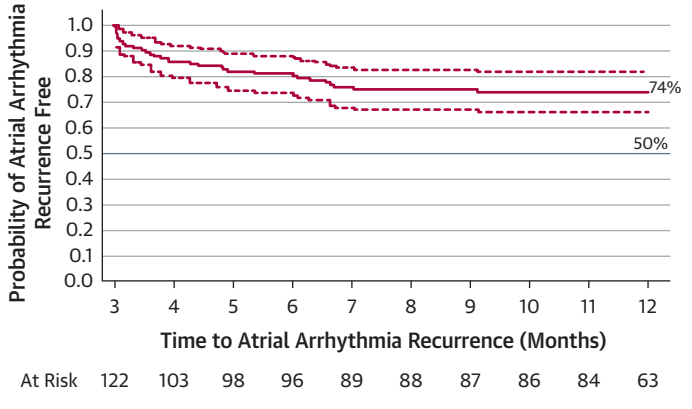

FIGURE 2 Kaplan-Meier Curve of Time to First Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia Recurrence (Effectiveness Cohort, n = 122)

Probability of freedom from symptomatic atrial arrhythmia recurrence at 12-month follow-up visit.

TABLE 2 Success Rate After Single Ablation Procedure and Off Drugs (Effectiveness Cohort)

	Failure	Success [95% Confidence Interval]
Cohort*	40 (34.2)	77 (65.8) [56.7%–74.3%]
Reason for failure		
AF recurrence post blanking	31 (26.5)	
No AF recurrence post blanking	9 (7.7)	
Repeat ablation	6 (5.1)	
On Class I/III AAD at 12 months	4 (3.4)	

Values are n (%). *The cohort (n = 117) consists of 122 patients in the effectiveness cohort minus the 5 patients who were lost to follow-up and were censored/excluded from the analysis.

AAD = antiarrhythmic drug; AF = atrial fibrillation.

(2 hematoma without intervention; 2 arteriovenous fistula requiring surgical repair).

The average CF was dichotomized at the median of 14 g; 84.6% of procedure-related major adverse events occurred among patients with CF ≥14 g (p = 0.0370). Multivariate logistic regression analysis showed that average CF ≥14 g was not significantly correlated with procedure-related major adverse events. Further analyses including only adverse events that are reasonably associated with radiofrequency application (i.e., tamponade and pericarditis) showed that the correlation remained insignificant in both univariate and multivariate analyses.

The 4 tamponade cases all had a percentage of time with CF ≥40 g >2.1% during radiofrequency applications. Due to the limited number of tamponade events, the correlation was only of borderline significance (p = 0.0581).

Patients who underwent radiofrequency ablation showed improved QOL in the mental and physical components of the Short Form Health Survey Version 2 instrument irrespective of effectiveness outcome. The mean mental and physical component scores were significantly higher at the 3-month follow-up visit compared to baseline (7.2 ± 9.89 [p < 0.0001] and 2.6 ± 6.74 [p < 0.0001], respectively). The increased QOL scores remained relatively constant through the 12-month follow-up visit (8.1 ± 11.19 [p < 0.0001] and 3.5 ± 6.74 [p < 0.0001], respectively).

Similarly, the mean symptom frequency and severity scores were significantly lower at the 3-month follow-up compared to baseline (-10.5 ± 10.27 [p < 0.0001] and -9.1 ± 8.17 [p < 0.0001], respectively) and remained relatively constant through the 12-month follow-up visit (-10.0 ± 9.84 [p < 0.0001] and -8.2 ± 8.30 [p < 0.0001], respectively).

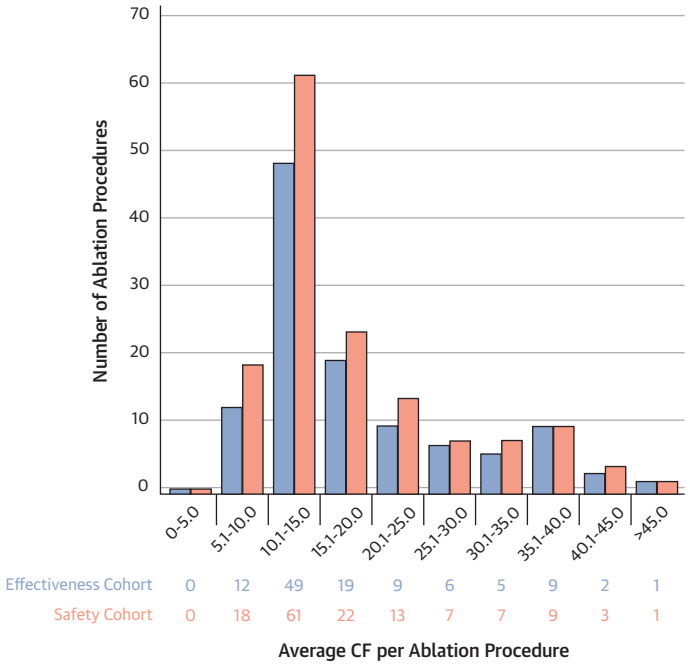

FIGURE 3 Distribution of Average CF

Histogram distribution of the average contact force (CF) used during radiofrequency application with average CF shown in 5-g increments (effectiveness cohort, n = 122; safety cohort, n = 161; data was unavailable or unanalyzable for 19 subjects).

DISCUSSION

The SMART-AF trial was the first prospective, multicenter clinical trial conducted to evaluate the safety and effectiveness of an irrigated CF-sensing catheter in patients with drug-refractory PAF. The 12-month effectiveness success rate (freedom from symptomatic atrial arrhythmia recurrence) was 74%. There were no unanticipated device-related adverse events. The contribution of real-time CF sensing to the ablation outcome was demonstrated by the significantly higher success rate (probability of freedom from recurrence of 81% vs. 66%) in patients where the investigators stayed within their selected CF range ≥80% of the time during radiofrequency application, suggesting that consistent and stable catheter-tissue contact is necessary for effective ablation results. In addition, these outcomes are accompanied by clinically meaningful improvement in QOL and AF symptoms/severity. Nevertheless, this is the first study of its kind, and the results will need to be confirmed in future randomized, controlled trial against traditional non-CF-sensing irrigated catheters (Central Illustration).

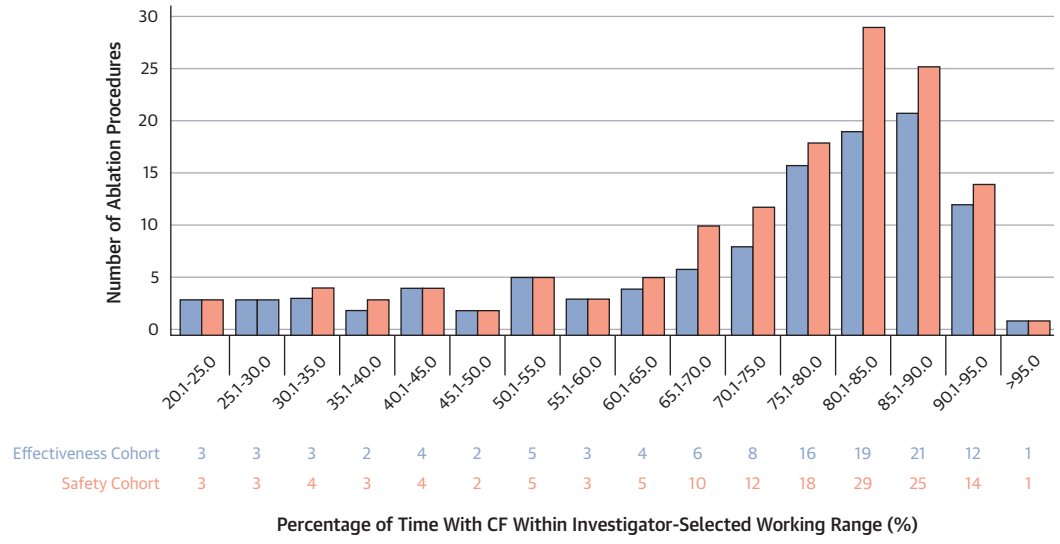

FIGURE 4 Distribution of Percentage of Time With CF Within Investigator-Selected Working Range

Percentage of time investigators spent in their selected ranges during radiofrequency applications (effectiveness cohort, n = 122; safety cohort, n = 161; data was unavailable or unanalyzable for 19 subjects). CF = contact force.

In this study, even with a rigorous definition of per-protocol effectiveness endpoint, the ablation outcome appears to be higher than previously reported in the study with similar patient population and study protocol using the traditional ThermoCool Catheter without CF (KM analysis 72.5% [current study, included symptomatic AF/AT/AFL recurrences] vs. 66% [traditional ThermoCool Catheter study, included symptomatic AF recurrence only], respectively) (12). However, a direct comparison was not conducted. In addition, a recent meta-analysis reported that the single-procedure success rate for PAF ablation was 66.6% (95% CI: 58.2% to 74.2%) (13). This meta-analysis included on- or off-drug success rates per individual study definition. In comparison, the single-procedure success rate off drug in our study was 65.8%, and slightly higher at 68.4% if including off- or on-drug patients.

These data strongly support the notion that real-time CF sensing is important in optimization of long-term ablation outcomes. This aligns with a recent publication showing that operators who ablated with real-time CF data available had lower acute PV reconnection rates than operators blinded to the CF information (14). PV reconnection has been shown to be an important factor contributing to mid- and long-term recurrence (15,16). In a long-term study, 94% of the patients who underwent a second ablation procedure had recovered PV conduction (16). In our study, repeat ablation procedures without recurrence during the effectiveness period was approximately 5% (6 of 122), which is substantially lower in comparison to the 20% to 40% reported in the expert consensus statement (1). Taken together, it is conceivable that real-time visualization of CF during radiofrequency applications reduces PV reconnection

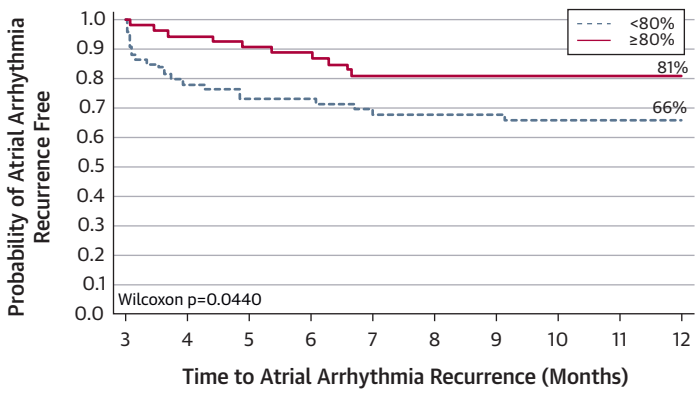

FIGURE 5 Kaplan-Meier Curve of Time to First Atrial Fibrillation/Atrial Flutter/Atrial Tachycardia Recurrence Through 12 Months

Investigators working in their selected ranges ≥80% of the time during radiofrequency application demonstrated a significant increase of 15% in the effectiveness success at 12 months compared to those working in their selected ranges <80% of the time (effectiveness cohort, n = 122).

TABLE 3 Multivariate Logistic Regression Analyses of Risk Factors for Primary Effectiveness Endpoint (Effectiveness Cohort, n =122)

Risk Factor	Odds Ratio	95% Confidence Interval	p Value*
Total procedure time, min	0.99	0.99–1.00	0.0340
Percentage of time with CF within investigator selected ranges ≥80%	4.25	1.53–11.79	0.0054
Percentage of time with lateral CF >30 g	1.16	0.94–1.42	0.1670
Percentage of time with shaft proximity interference severity ≥2	0.99	0.97–1.01	0.3797

*Analysis was based on subjects with nonmissing data for outcomes and risk factors.

by creation of durable lesions, leading to fewer repeat procedures and improved success rate, without compromising the safety profile or prolonging the procedure time. However, this remains to be proven.

A recent study using a different CF-sensing catheter system found that AF patients ablated with >20 g average CF had lower recurrence at 12-month follow-up (5). Although the overall average procedural CF during radiofrequency application in our study was found to be similar to that reported using the alternative CF-sensing catheter (6) (17.9 ± 9.42 g vs. 17.2 ± 13.5 g, respectively), our data did not indicate a correlation between higher average procedural CF and effectiveness outcomes. The difference may be due to a larger study population, different catheter design, and user instructions, as well as an increased number of operators with unique techniques in our study. More importantly, our study operators were never blinded to the CF at any time during the procedure. Therefore, direct comparison of CF data from our study to the previous study may be difficult.

Another interesting finding of our study shows that the percentage of time the investigator stayed within their selected working range (regardless of the range selected) correlated positively with primary effectiveness success. Specifically, multivariate analyses showed that investigators who stayed within their selected ranges ≥80% during radiofrequency application were approximately 4.25 times more likely to have effectiveness success at 12 months compared with those who did not (95% CI: 1.53 to 11.79). These data suggest that maintaining catheter-tissue contact stability by maintaining the CF within user selected range during ablation therapy increases the likelihood that the radiofrequency power will be effectively deposited within the tissue and not the surrounding blood pool, and this in turn, could be critical to achieving long-term success.

Our study demonstrates an acceptable safety profile of AF ablation with the irrigated CF-sensing catheter. Notably, there were no deaths, stroke, cerebrovascular accident, atrioesophageal fistula, myocardial infarction, thromboembolism, or PV stenosis within the study period. The cardiac tamponade rate (2.48%) fell within the typical range published in the literature (1,17,18). Among AF ablation reports reviewed for the 2012 Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society Expert Consensus Statement, cardiac tamponade had an incidence of up to 6% (1). Cappato et al. (17) reported tamponade rates of 1.2% (2005) (18) and 1.3% (2010) in 2 worldwide surveys of AF procedures. Another large series reported cardiac tamponade during 15 of 632 ablation procedures (2.4%) (19). In this study, there was a trend toward greater percentage of time in higher CF (≥40 g) for all the tamponade cases, but the correlation was not statistically significant, likely due to the limited number of events reported.

It has been suggested that visualization of the applied CF or catheter-tissue contact during the ablation procedure could help reduce occurrence of certain ablation complications without loss of lesion effectiveness (7). In our study, average CF ≥14 g was not significantly correlated with procedure-related major adverse events in the final multivariate analysis. Further studies with a larger sample size would allow us to better understand the correlation of CF with safety outcomes.

Durable long-term effectiveness is the ultimate goal of AF catheter ablation. A recent study found that long-term recurrences in patients who received AF ablation were common, even among those who were arrhythmia free at 1-year post-ablation, and that early recurrences were the strongest predictor of late recurrences (20). These findings highlight the need to improve lesion formation and consistency

Dataset	No. of Pts	12-Month Success (AF/AT-free)
SMART-AF (≥80% time within preselected contact force range)	51	81%
SMART-AF (<80% time within preselected contact force range)	57	66%
Non Force-Sensing Open-Irrigated Catheter*	106	66%

CENTRAL ILLUSTRATION Outcomes Comparison With Various Types and Forces of Ablation Catheters

Twelve-month success rates, defined as freedom from atrial fibrillation (AF) and/or atrial tachycardia (AT) events, with various types and forces of ablation catheters. *Data for this row from Wilber (12).

to reduce PV reconnection. It has been known that low electrode-tissue CF is associated with ineffective lesion formation (7). Our study provided the first clinical outcomes of AF ablation using this CF-sensing catheter, which showed a good medium-term success without compromising the safety profile.

STUDY LIMITATIONS. This 1-arm, open-label study compared safety and effectiveness endpoints with historical performance goals. No control group was assessed. The analysis of clinical outcome as a function of how often the force stayed within the prescribed interval was a post-hoc analysis, and should be considered hypothesis-generating only. Because the force-power-time index and lesion depth were not measured, the exact mechanism of improved success rate through maintaining stable CF warrants further research. Patients with significant left ventricular dysfunction, more persistent forms of AF, and advanced degrees of heart failure were excluded from the study, meaning our results may not be extrapolated to these populations. In the logistic regression models, forward selection method was used to select potential predictors for the outcomes. Given the low event rates compared with the number of covariates entered into the forward selection procedure, these analyses should be regarded as exploratory and considered hypotheses generating for follow-up studies.

CONCLUSIONS

The SMART-AF study demonstrates that ablation with a novel CF-sensing catheter is safe and effective for the treatment of drug refractory symptomatic PAF with clinically meaningful improvement in QOL and symptom severity/frequency, and no unanticipated device-related adverse events. Stable CF during radiofrequency application increases the probability of a successful procedure outcome. Investigators spending ≥80% of their radiofrequency ablation time in their user-selected CF ranges were approximately 4.25 times more likely to have primary effectiveness success at 12 months compared with those subjects with CF <80% of the time within the selected ranges. However, average CF during the procedure was not found to correlate with increased procedural success and procedure-related serious adverse events, such as cardiac tamponade.

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REPRINT REQUESTS AND CORRESPONDENCE: Dr. Andrea Natale, Texas Cardiac Arrhythmia Institute at St. David's Medical Center, 3000 N. IH-35, Suite 700 (705Res Foundation), Austin, Texas 78705. E-mail: dr.natale@gmail.com.

PERSPECTIVES

CLINICAL COMPETENCY IN PATIENT CARE: Atrial fibrillation (AF) ablation is more effective than antiarrhythmic drug therapy in maintaining normal sinus rhythm in patients with paroxysmal AF.

COMPETENCY IN PROCEDURAL SKILLS: A contact force sensing catheter helps obtain stable catheter-to-cardiac tissue contact during AF ablation, substantially improving 12-month freedom from AF recurrence.

TRANSLATIONAL OUTLOOK 1: The mechanism of improved outcomes derived from contact force sensing catheters for AF ablation, and specifically the interaction between contact force, catheter stability, duration and efficacy of ablation needs further examination to facilitate the further refinement of ablation apparatus.

TRANSLATIONAL OUTLOOK 2: A longer term study including a wider variety of patients with AF is needed to confirm and assess the generalizability of the findings of this study.

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KEY WORDS atrial fibrillation, catheter ablation, contact force, radiofrequency

APPENDIX For a list of the clinical sites and principal investigators, please see the online version of this article.