Randomized, Controlled Trial of the Safety and Effectiveness of a Contact Force–Sensing Irrigated Catheter for Ablation of Paroxysmal Atrial Fibrillation

Results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) Study

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Background—Contact force (CF) is a major determinant of lesion size and transmurality and has the potential to improve efficacy of atrial fibrillation ablation. This study sought to evaluate the safety and effectiveness of a novel irrigated radiofrequency ablation catheter that measures real-time CF in the treatment of patients with paroxysmal atrial fibrillation.

Methods and Results—A total of 300 patients with symptomatic, drug-refractory, paroxysmal atrial fibrillation were enrolled in a prospective, multicenter, randomized, controlled trial and randomized to radiofrequency ablation with either a novel CF-sensing catheter or a non-CF catheter (control). The primary effectiveness end point consisted of acute electrical isolation of all pulmonary veins and freedom from recurrent symptomatic atrial arrhythmia off all antiarrhythmic drugs at 12 months. The primary safety end point included device-related serious adverse events. End points were powered to show noninferiority. All pulmonary veins were isolated in both groups. Effectiveness was achieved in 67.8% and 69.4% of subjects in the CF and control arms, respectively (absolute difference, −1.6%; lower limit of 1-sided 95% confidence interval, −10.7%; \( P = 0.0073 \) for noninferiority). When the CF arm was stratified into optimal CF (≥90% ablations with ≥10 g) and nonoptimal CF groups, effectiveness was achieved in 75.9% versus 58.1%, respectively (\( P = 0.018 \)). The primary safety end point occurred in 1.97% and 1.40% of CF patients and control subjects, respectively (absolute difference, 0.57%; upper limit of 1-sided 95% confidence interval, 3.61%; \( P = 0.0004 \) for noninferiority).

Conclusions—The CF ablation catheter met the primary safety and effectiveness end points. Additionally, optimal CF was associated with improved effectiveness.

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Multiple randomized, clinical trials have demonstrated that catheter ablation is superior to antiarrhythmic medications for the treatment of paroxysmal atrial fibrillation (AF). Although conceptually straightforward, the placement of continuous point-by-point radiofrequency ablation lesions around the pulmonary veins (PVs) is technically challenging. Achieving a continuous ring of atrial necrosis without conduction gaps can be difficult. Although acute electrical PV isolation is almost universally achieved eventually, the mechanism of acute isolation is typically a combination of myocardial necrosis and a significant degree of tissue edema, often resulting in reversible injury. With resolution of reversible injury, PV reconnections occur and may again result in AF. Indeed, long-term follow-up studies of AF patients who underwent PV isolation show continued attrition of efficacy over time, resulting predominantly from PV reconnections in the vast majority. Durable PV isolation can be an elusive goal.
Technical limitations in point-by-point radiofrequency energy delivery have prompted intense development to improve the tools used to achieve durable PV isolation. A limitation of standard radiofrequency ablation has been the inability to directly assess the degree and quality of contact between the catheter tip and target tissue, prompting operators to rely on surrogate markers of contact such as baseline impedance, impedance change, electrode temperature, and catheter location by fluoroscopy or electroanatomic mapping.9-11 Lesion formation depends on a combination of radiofrequency power, duration, and contact force (CF), but CF has not been measurable thus far. Recently, ablation catheters have been introduced that have the capability to quantify the CF between the catheter tip and tissue in real time.12-16 In preclinical studies, a direct relationship between the CF measured by these catheters and lesion size that is independent of delivered radiofrequency power has been established.14,15,17 In addition, a lesion with poor CF may lead to edema without a durable lesion but make the creation of a durable lesion more difficult. Furthermore, several nonrandomized, clinical studies have demonstrated the potential benefit of knowing and applying CF information during AF ablation.12,13,16 These studies have set the stage for a multicenter, prospective, randomized, controlled trial comparing a CF-sensing catheter with a standard catheter with respect to safety and efficacy.

Methods

The TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) study was a prospective, randomized, controlled, multicenter study conducted to evaluate the safety and effectiveness of the CF catheter (TactiCath, St. Jude Medical, St. Paul, MN) for the treatment of symptomatic paroxysmal AF. The study, conducted under an Investigational Device Exemption for regulatory approval, was designed as a noninferiority trial for safety and effectiveness. It was not powered for superiority. Subjects were enrolled at 17 clinical sites and treated by 47 operators in Europe and the United States. The Ethics Committee or Institutional Review Board of each participating institution approved the study protocol, and written informed consent was obtained from all patients. An independent Data Safety Monitoring Board supervised the study.

Patient Selection

Patients with symptomatic, paroxysmal AF that was refractory or intolerant to at least 1 class I to IV antiarrhythmic drug (AAD) who were planned for catheter ablation were eligible for participation in the study. Subjects were required to have at least 1 documented episode of AF >30 seconds and a minimum of 3 episodes documented by history within the 12 months before enrollment. Key exclusion criteria included persistent AF, myocardial infarction within the 3 months before the intervention, prior left atrial ablation (surgical or catheter), left atrial diameter >5 cm, left ventricular ejection fraction <35%, contraindications to long-term antithrombotic therapy, and severe pulmonary disease.

Treatment Arms

Patients were randomized in a 1:1 ratio to catheter ablation with either the TactiCath CF catheter or a control catheter (ThermoCool Navistar, Biosense Webster, Diamond Bar, CA). The catheters are dimensionally equivalent and were designed with 6 holes for open irrigated radiofrequency ablation. They also have a multielectrode design with a deflectable tip, allowing monitoring of intracardiac signals and pacing capabilities. The distinguishing feature of the CF catheter is the 3 fiberoptic sensors located at a 120° angle from each other within the tip. These sensors measure microdeformations that correlate to the applied CF between the catheter tip electrode and the underlying tissue.14,15 These small fiberoptic lines allow force to be measured very close to the tip. The TactiSys system (St. Jude Medical) displays detailed CF information by determining the cross-product of axial and lateral force components to obtain the resultant force vector, fully describing the force at the point of contact between the catheter and tissue surface. The system displays the calculated force-time integral, which is determined from the CF and the duration of radiofrequency application during ablation.15 The 3-dimensional (3D) electroanatomic mapping system used was dictated by the labeling of each device. For subjects randomized to the CF catheter, the EnSite NavX electroanatomic mapping system (St. Jude Medical) was used. For control subjects undergoing ablation with the control catheter, the CARTO electroanatomic mapping system (Biosense Webster) was used.

To allow for initial familiarization with the CF device, up to 2 subjects per site were enrolled as roll-in patients.

Catheter Ablation Procedure

The index procedure involved isolation of all PVs performed according to the physician’s standard practice. Acute electrical PV isolation was confirmed by the presence of entrance block 30 minutes after complete isolation of all PVs. Additionally, isoproterenol-induced latent PV conduction and non-PV triggers were identified and ablated at the physician’s discretion. Additional lines and complex fractionated atrial electrograms were targeted at the physician’s discretion. Ablations were performed with the minimum radiofrequency power deemed necessary by the operator and with a standardized, power-dependent irrigation rate. When the study device was used, the CF and derived parameters were provided to the operator in real time and recorded throughout the procedure.

Importantly, no target CF guidelines were specified by the protocol, and CF application during this study was based on clinical data from other studies that became available as this study progressed. The protocol allowed additional left atrial ablations to treat known or suspected arrhythmia triggers, provided that the catheter assigned by randomization was used. A right atrial isthmus line ablation was recommended if atrial flutter was documented either before or during the procedure.

Follow-Up

Patients were followed up for 12 months after the index procedure and evaluated with office visits at 7 days and 3, 6, and 12 months after the initial ablation. During the 3-month blanking period after the index procedure, a maximum of 2 repeat ablation procedures were allowed with the catheter type assigned at the index procedure. During the blanking period, the use of AADs was allowed, but all class I and III AADs were to be discontinued at the end of the blanking period.

Transthoracic monitoring (TTM) was required after the blanking period with weekly transmissions until 5 months after ablation, followed by monthly transmissions. Subjects transmitted additional unscheduled TTM whenever symptoms recurred. Ambulatory 24-hour Holter monitoring was performed at the end of the study. All TTM were evaluated by an independent core laboratory.

Study End Points

The primary effectiveness end point reflected the combined short- and long-term ablation success. Acute ablation success was defined as complete isolation of all PVs at the end of the index procedure. Long-term ablation success was defined as freedom from recurrence of symptomatic AF, atrial tachycardia, or atrial flutter at 12 months after the index procedure off AADs, with the exclusion of the 3-month blanking period. Any acute procedural failure, retreatment with ablation, use of class I or III AAD, or symptomatic recurrence documented by TTM or ECG after the blanking period constituted treatment failure. Unlike other recently reported studies, use of any class I or III AAD beyond the 3-month blanking period was considered a failure even if no AF was documented.13,14
A worst-case sensitivity analysis was performed on the modified intention-to-treat population. The modified intention-to-treat population included all randomized patients in whom a study device was introduced and PV isolation was attempted. The worst-case situation imputed failures for subjects who terminated early without failure from the study arm and imputed successes for subjects who terminated early without failure from the control arm.

An alternative definition of treatment success, referred to as clinically relevant effectiveness, was also used to provide a more clinically meaningful measure of effectiveness. The differences between primary and clinically relevant effectiveness failure consist of the following: Failure resulting from AAD use after blanking needs to be associated with documentation of arrhythmia through TTM or ECG, and failure resulting from TTM only required at least 3 positive TTMs.

The primary safety end point included device-related serious adverse events occurring within 7 days of the index procedure or hospital discharge, whichever was later. Events were classified as primarily device or procedure related and adjudicated by an independent Clinical Events Committee. Only patients in whom a catheter was introduced during the index procedure were included in the analysis of the safety end point (safety population; Figure 1).

Secondary Analyses

A CF ≥10 g was retrospectively considered optimal during the creation of radiofrequency lesions. This was based on data generated as this study was ongoing that demonstrated a high percentage of ineffective PV isolation lesions with a low CF. Therefore, ablation results were evaluated for 2 complementary patient groups: patients with ≥90% of their lesions created with a CF ≥10 g (optimal CF group) and patients with <90% of the lesions created with a CF ≥10 g (nonoptimal CF group).

The patient’s quality of life was assessed at baseline and at the 12-month follow-up with the Atrial Fibrillation Effect on Quality of Life questionnaire. This questionnaire enables evaluation of the overall score and 3 subareas: symptoms, daily activities, and treatment concerns. Comparisons were made between the catheter types and between patients with a successful outcome and those with an ablation failure.

The use of the 3D mapping system was linked to the subject’s randomization. To evaluate the potential for operator bias resulting from experience related to the mapping system, operators were asked anonymously to rate their prior experience with the EnSite NavX and CARTO 3D mapping systems. Rating was relative to EnSite NavX system experience, with 50% showing equal experience with both 3D mapping systems. Ratings were averaged per center and weighted by the number of patients treated by the center. The impact of prior experience with either 3D mapping systems on the protocol-defined success rate was evaluated.

**Statistical Methods**

Statistical analysis was performed to evaluate the noninferiority of the study device compared with the control with respect to the primary safety and effectiveness end points. Noninferiority margins of 9% and −15% were used for the analysis of the safety and effectiveness end points. One-sided 95% confidence limits for the risk difference of TactiCath minus control (lower limit for effectiveness, upper limit for safety) were calculated with the Farrington-Manning approach. In addition, P values for noninferiority testing with the Farrington-Manning test were provided. Noninferiority margins agreed with the US Food and Drug Administration specifications before the study.

For the sample size calculations related to the primary effectiveness end point, the treatment success rate in both treatment groups was assumed to be ≈55% on the basis of previous studies. A total of 274 patients provides 80% power to show noninferiority with a noninferiority margin of −15% and a 1-sided 5% significance level. For the primary safety end point, the incidence of primary serious adverse events within 7 days of the index procedure was expected to be 9% in both treatment arms. A total of 274 patients provides 83% power to show noninferiority with a noninferiority margin of 9% and a 1-sided 5% significance level. Sample size was increased by 10% to account for attrition, resulting in a total of 300 randomized subjects.

To investigate potential treatment differences across study centers, a logistic regression analysis for treatment success was performed that included treatment, center, and treatment-by-center interaction as explanatory variables.

Categorical variables are expressed as counts and percentages and were compared with the Fisher exact test. Continuous variables are
reported as mean±SD or median when relevant and were compared by use of the Mann-Whitney U test. One-sided tests were used in comparisons involving the optimal CF group. Two-sided tests were used otherwise. A value of \( P < 0.05 \) was considered to be statistically significant.

**Results**

A total of 317 patients were enrolled in this study, of whom 17 were roll-in patients (Figure 1). Of the 300 patients who were randomized, 5 patients were excluded from analysis because no ablation was performed. The remaining 295 patients were included in the analysis of the primary safety end point (safety population). Patients in whom PV isolation was attempted and who had no major protocol deviations (\( n=280 \)) were analyzed for the effectiveness end points (146 and 134 patients were treated with the CF and control catheters, respectively).

**Patient Characteristics**

Baseline patient demographics of the 295 patients who make up the safety population are summarized in Table 1. The mean age of all patients was 60.3±10.1 years, and 64.7% were male. The mean left atrial diameter and left ventricular ejection fraction were 39.6±5.2 mm and 62.5±6.7%, respectively. A history of structural heart disease was present in 5.8% of patients. There were no significant differences between the patients assigned to each treatment arm.

**Procedural Characteristics**

The median fluoroscopy and radiofrequency ablation times were 27.0 versus 23.0 minutes (\( P=0.044 \)) and 46.5 versus 53.0 minutes (\( P=0.018 \)) for the CF group versus the control group, respectively. During the 30-minute waiting period, 12.1% of lesions sets had PV reconnections, 10.4% in CF group versus 13.8% in the control group (\( P=0.206 \)). Ultimately, all PVs were electrically isolated in both treatment groups.

**Effectiveness End Point**

Short-term ablation success was achieved in 100% of patients in both treatment groups in that all targeted PVs were successfully electrically isolated. The primary effectiveness end point at 12 months was achieved in 67.8% and 69.4% of the CF and control group, respectively (absolute difference, −1.6%; lower limit of 95% confidence interval, −10.7%; \( P=0.0073 \) for noninferiority), which was above the predefined noninferiority margin of −15% (Figure 2A). The study end point was also met even under the worst-case conditions of the modified intention-to-treat population (290 patients). Clinically relevant success at 12 months was achieved in 78.1% and 80.6% of the patients in the CF and control group, respectively (\( P=0.659 \); Figure 2B). To allow comparison with historical studies, including the recently reported ThermoCool Smarttouch Catheter for the Treatment of Symptomatic Paroxysmal Atrial Fibrillation (SMART AF) study, an additional analysis was retrospectively performed by applying the definition of a protocol-defined success but allowing previously failed AAD during the effectiveness period (on-drug analysis). With this approach, success rates of 72.6% and 73.9% were achieved with the study device and the control device, respectively. For the primary end point, no treatment difference was detected across study centers (\( P=0.20 \) for treatment-by-center interaction term).

<table>
<thead>
<tr>
<th>Table 1. Demographics of All Patients in the Safety Population</th>
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<tbody>
<tr>
<td>CF Catheter (( n=152 ))</td>
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<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Male sex, ( n ) (%)</td>
</tr>
<tr>
<td>Coronary artery disease, ( n ) (%)</td>
</tr>
<tr>
<td>Heart failure, ( n ) (%)</td>
</tr>
<tr>
<td>Hypertension, ( n ) (%)</td>
</tr>
<tr>
<td>Diabetes mellitus, ( n ) (%)</td>
</tr>
<tr>
<td>Stroke or TIA, ( n ) (%)</td>
</tr>
<tr>
<td>Structural heart disease, ( n ) (%)</td>
</tr>
<tr>
<td>AADs at baseline, ( n ) (%)</td>
</tr>
<tr>
<td>Left atrial diameter, mm</td>
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<td>LVEF, %</td>
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Values are mean±SD when appropriate. AAD indicates antiarrhythmic drug; CF, contact force; LVEF, left ventricular ejection fraction; and TIA, transient ischemic attack.

**Figure 2.** Kaplan–Meier survival curves with respect to protocol-defined and clinically relevant success. A, Primary effectiveness success for contact force (CF; study device) and control catheters (control device). B, Clinically relevant success for the 2 groups. C, Primary effectiveness success for the optimal and nonoptimal CF groups. D, Clinically relevant success for the optimal and nonoptimal CF groups.
Thirty-three subjects (11.8%) underwent a repeat ablation procedure during the assessment period after blanking (16 CF, 17 control). One subject in the control arm required a third procedure. There were 12 subjects with repeat ablation during the blanking period (6 in each treatment arm).

Optimal Versus Nonoptimal Contact Force
On retrospective analysis, data suggested that, when ≥90% of the lesions were created with a CF ≥10 g, there appeared to be more durable PV isolation. During PV isolation with the CF catheter, an optimal CF (≥90% of the lesions created with a CF ≥10 g) was achieved in 57.2% of the patients. Ablation with optimal CF resulted in significantly higher success rates compared with results from PV isolation with nonoptimal CF. The protocol-defined success was 75.9% for optimal CF versus 58.1% for nonoptimal CF groups (P=0.018). The clinically relevant success rate was 85.5% versus 67.7% for those with optimal CF compared with those with nonoptimal CF (P=0.009; Figure 2C and 2D). There were no statistically significant differences between optimal and nonoptimal CF patients in terms of the baseline characteristics as reported in Table 1. In the on-drug analysis, the success rate was 79.5% in the optimal CF group versus 58.1% in the nonoptimal CF groups (P=0.018). The clinically relevant success rate was 85.5% versus 67.7% for those with optimal CF compared with those with nonoptimal CF (P=0.009; Figure 2C and 2D). There were no statistically significant differences between optimal and nonoptimal CF patients in terms of the baseline characteristics as reported in Table 1. In the on-drug analysis, the success rate was 79.5% in the optimal CF group versus 58.1% in the nonoptimal CF group (P=0.022). There was a trend toward a lower rate of repeat ablations in the optimal CF group compared with the nonoptimal CF group (7.2% versus 12.7%; P=0.148).

Among the 36 operators who used the study device, 10 operators achieved an optimal CF in all of their patients, whereas 13 operators did not achieve optimal CF in any of their patients (Figure 3A). Operators who realized an optimal CF in >80% of their patients achieved a significantly higher protocol-defined success rate than the others (79.1% versus 58.2%; P=0.008; Figure 3B). CF was significantly different (26.5 g versus 19.2 g; P<0.001) between the 2 groups (Figure 3C). Interestingly, the mean power in the group that used optimal CF was also lower (28.0 versus 26.9 W; P<0.001). Although this difference is slight, it suggests that optimal CF may allow less power.

Impact of Experience With the 3D Mapping System
Before entry in the study, sites were required to demonstrate comparable proficiency with both of the 3D mapping systems used in the study. Surveys indicated that the experience with the EnSite NavX system was proportionately lower (42.0±23.2%), showing a trend toward more experience with CARTO (58.0±23.2%), which was used in all control catheter cases. Experience ratings were divided into 4 categories with approximately similar numbers of patients in each category (Figure 4). Operators with far below-average experience with the EnSite system (lowest group in Figure 4) achieved a significantly lower protocol-defined success rate with the study device than those with average or above-average experience with the EnSite system (P=0.002). For the least experienced EnSite system operators, treatment success occurred in 47.5% of patients compared with 75.7% (P=0.019) in those with equivalent experience and 80.0% (P=0.004) in those with more EnSite system experience.
There were a total of 77 patients (40 CF, 37 control) treated by operators with <25% EnSite experience. When these patients were excluded from the primary effectiveness analysis, the success increased from 67.8% to 76.0% in the CF group and from 69.4% to 69.8% in the control group. Of course, because of the smaller sample size, the increased success observed in the CF group when the less experienced EnSite operators were excluded did not reach statistical significance.

**Quality of Life**

Quality-of-life changes from baseline to 12 months are presented in Figure 5. Significant quality-of-life improvements were observed in both arms with a nonsignificant trend for the CF versus control group. Overall, patients with a clinically relevant success showed a significantly higher improvement than those with a failure (P=0.002). This effect was stronger in the control arm compared with the CF arm (P=0.008 versus P=0.051). For the subcomponents, these effects were significant for the control device (except the symptoms component) and nonsignificant for the CF arm.

**Safety End Point**

There was no difference between the CF and control groups with respect to overall serious adverse events (device or procedure related), which occurred in 7.2% and 9.1% of patients, respectively (Table 2). The primary safety end point, which consisted of primary device-related serious adverse events, occurred in 1.97% and 1.40% of patients in the CF and control group, respectively (absolute difference, 0.57%; upper limit of 1-sided 95% confidence interval, 3.61%; P=0.0004 for noninferiority). This is below the predefined noninferiority margin of 9% and fulfilled the noninferiority criteria for safety. In the CF and control groups, 3 and 2 primary device-related serious adverse events occurred, respectively. There were no deaths, strokes, transient ischemic attacks, or atrioesophageal fistulas in either group.

**Discussion**

Here, we report the first prospective, multicenter, randomized, controlled trial comparing a real-time CF-sensing irrigated radiofrequency ablation catheter (TactiCath) with a standard irrigated radiofrequency ablation catheter (ThermoCool Navistar). In the trial, 300 patients with drug-refractory paroxysmal AF were randomized in a 1:1 manner to undergo PV isolation with either a force-sensing or non–force-sensing catheter. Both the primary effectiveness and primary safety end points for noninferiority of the CF catheter versus the control catheter were met. These end points fulfilled noninferiority criteria even when the more recent and stringent 1-sided confidence interval margins of 97.5% for the risk difference (−12.4% for primary effectiveness and 4.42% for primary safety end point) were used.

**Ablation Efficacy**

Acute procedural success was achieved in all patients, with 100% of targeted PVs being successfully isolated during the index procedure with both catheters. After the blanking period, the 12-month drug-free rate of freedom from atrial arrhythmias was 67.8% for the CF group versus 69.4% for the control group (P=0.0073 for noninferiority). Several factors may have contributed to the failure of the CF catheter to demonstrate superior efficacy compared with the control catheter. First, this study was designed to demonstrate noninferiority rather than superiority, and a much larger sample size would have been necessary to demonstrate superiority. Two other important factors are the lack of optimal CF delivery during the study and operator effect.

**Optimal CF**

The study protocol did not specify CF guidelines for ablation. However, during the conduct of the TOCCASTAR study, clinical results from other concurrent CF studies became available and were shared with operators. These studies provided optimal CF guidelines that were then incorporated by some operators during this study. Therefore, not all patients in this study underwent ablation according to these optimal CF parameters, and this may have partially accounted for the lack of superiority of the CF catheter in this study. That is, one cannot reasonably expect a tool to enhance a procedure if the tool is not being used optimally.

**Table 2. Serious Adverse Events**

<table>
<thead>
<tr>
<th>Category of SAEs</th>
<th>CF Catheter (n=152), n (%)</th>
<th>Control Catheter (n=143), n (%)</th>
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<tbody>
<tr>
<td>Device-related SAEs (primary)</td>
<td>3 (1.97)</td>
<td>2 (1.40)</td>
</tr>
<tr>
<td>Cardiac tamponade/perforation</td>
<td>1 (0.66)</td>
<td>1 (0.70)</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>2 (1.32)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Pulmonary vein stenosis</td>
<td>0 (0.0)</td>
<td>1 (0.70)</td>
</tr>
<tr>
<td>Procedure-related SAEs</td>
<td>10 (6.58)</td>
<td>11 (7.69)</td>
</tr>
<tr>
<td>Cardiac tamponade/perforation</td>
<td>1 (0.66)</td>
<td>1 (0.70)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>2 (1.32)</td>
<td>2 (1.40)</td>
</tr>
<tr>
<td>Vascular access complications</td>
<td>3 (1.97)</td>
<td>3 (2.10)</td>
</tr>
<tr>
<td>Hospitalizations (initial or prolonged)</td>
<td>4 (2.63)</td>
<td>5 (3.50)</td>
</tr>
<tr>
<td>Total device- and procedure-related SAEs</td>
<td>11 (7.24)*</td>
<td>13 (9.09)</td>
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CF indicates contact force; and SAE, serious adverse event.

*Two patients in the CF group had device- and procedure-related events.
Optimal CF parameters were based on several studies, including EFFICAS I in which operators were blinded to CF information while performing PV isolation. Results showed that PV reconnections were more frequent in segments with lower CF and force-time integral after an invasive mapping procedure at 3 months.\(^{16}\) Based on data gleaned from this study, EFFICAS II was conducted and provided unblinded operators CF guidelines for ablation (minimum CF ≥10 g, target CF ≥20 g, minimum force-time integral >400 grams-seconds). Comparing the PV reconnection rate at 3 months with that of the EFFICAS I patients showed that PV reconnections were decreased by 90% when CF guidelines were met (unpublished data). The TOCCATA study demonstrated that, when PV isolation was performed with an average CF <10 g, AF recurrence was 100%. When the average CF was >20 g, AF recurrence was reduced to 20% (\(P=0.01\)).\(^{12}\) Additionally, this study demonstrated that intermittent contact is more prevalent at low CF, which has implications for lesion quality. Together, these studies demonstrated that procedural success is highly dependent on achieving a minimum CF force during ablation and avoiding CF instability caused by intermittent contact.

On the basis of these observations, a retrospective analysis was performed in this study in which patients who had undergone ablation with optimal CF were compared with those who did not. In this analysis, optimal CF was defined as ≥90% of the lesions created with a CF ≥10 g. When the CF arm was divided into subgroups based on optimal CF versus nonoptimal CF, primary effectiveness success occurred in 75.9% versus 58.1% of subjects (\(P=0.018\)), and clinically relevant treatment success rate occurred in 85.5% versus 67.7% (\(P=0.009\)). This significant improvement in efficacy suggests an important finding related to the value of maintaining stable CF during radiofrequency delivery: Delivering more lesions at low CF significantly increases the risk for arrhythmia recurrence. Previous guidance and training have justifiably focused on the importance of positional stability of the catheter tip to achieve good lesions. However, positional stability does not guarantee stable CF, especially when the total force is <10 g and there is intermittent contact. The TOCCATA study has shown that stable CF is critically important to ensure treatment effectiveness. Because stable, optimal CF is associated with positional stability, operators should critically focus their attention on measures of CF stability during lesion creation.

**Operator Effect**

In this study, the CF achieved by operators was highly variable. In the CF arm, 12 operators achieved an optimal CF in their patients and a corresponding high rate of treatment success (79.1%). Additionally, subjects treated by these operators required lower radiofrequency power while achieving a better outcome. Finally, the rate of serious adverse events was somewhat lower in this group (6.0% versus 6.3%). These findings suggest that the use of CF may facilitate diligence in positioning the catheter before ablation and maintaining stable contact during radiofrequency, thus contributing to improved safety and efficacy.

Measures of procedural efficiency such as the rate of acute reconnection revealed that operators successfully maintained a low rate of acute reconnection throughout the trial at ≈11% of PVs in the CF arm. In contrast, the control group experienced a much higher rate of acute reconnection initially (18%), which was subsequently reduced to 9% at the end of trial. Although the acute reconnection rate is not uniquely correlated with treatment success, it appears that operators adapted their use of the control device on the basis of their experience with the CF catheter. Indeed, most operators anecdotally claimed this learning effect.

Relative equivalence in study outcomes between the 2 catheters may be accounted for partially by the relative operator experience with each mapping system. The primary goal of the TOCCASTAR trial was to compare the CF and control catheters. Because each catheter was linked to a different mapping system (control with CARTO, CF catheter with EnSite), this study was not a pure comparison of CF sensing and no CF sensing. The majority of AF ablations have historically been performed with the CARTO system; indeed, operators in this study tended to have less experience with the EnSite system. The primary effectiveness end point was much higher when operators had equivalent (75.7%; \(P=0.019\)) or more (80.0%; \(P=0.004\)) experience with the EnSite system compared with those with the least experience (47.5%) with this system. When the patients who were ablated by operators with the least EnSite experience (<25%) were excluded, primary effectiveness increased from 67.8% to 76.0%. Of course, this numeric difference did not reach statistical significance because of the smaller sample size.

Although both catheters were found to be equivalent, this study demonstrated that the efficacy may have been improved with the CF catheter if operators delivered optimal CF and were more experienced with the EnSite mapping system.

**Safety**

The safety profile of the CF catheter was similar to that of the control catheter. Both study arms experienced low rates of primary (device-related) safety events, which occurred in 1.97% of patients in the CF group and 1.40% in the control group (\(P=0.0004\) for noninferiority). The overall serious adverse event rates (device or procedure related) were also similar between the CF (7.2%) and control (9.1%) groups. Of those, there was 1 procedure-related and 1 device-related cardiac tamponade in each group (1.3% in the CF group and 1.4% in the control group). This rate is in line with other studies that report a cardiac tamponade rate of 0.9% to 1.3%.\(^{3,19,20}\) The recently published SMART-AF trial with another CF-sensing ablation catheter reported a higher cardiac tamponade rate of 2.5%.\(^{13}\) The reason for the differences in this complication rate between the 2 catheters is not clear but may be attributable to differences in catheter design and stiffness and in CF delivery. One subject in the control group had PV stenosis. There were no manifest cerebral thromboembolic events or atriointerphalgeal fistulas in either group.

The safety of the CF catheter compared favorably with prior studies.\(^{3,14,13}\) However, it is known that safety events can be related to excessive radiofrequency power or CF. In particular, prior preclinical investigations suggest that the incidence of steam pops increases at power >30 W or CF>30 g.\(^{14,17,21}\) Although there was no specific recommendation in the TOCCASTAR protocol as to the force or power that should
be used, the manufacturer recommends that power be limited to 30 W and CF to 30 g in AF ablation, largely on the basis of prior published data. Most users in this study were generally experts with experience of several hundreds of AF ablations. However, it is possible that the use of optimal CF (in particular, keeping CF <30 g) may reduce complications among less experienced users.

Conclusions
This prospective, multicenter, randomized, controlled trial demonstrated that the CF-sensing ablation catheter was noninferior to the standard non–force-sensing catheter with respect to short- and long-term efficacy and safety. The trial also demonstrated that operator effects related to adherence to optimal CF guidelines and the use of a 3D mapping system may positively influence overall outcomes of AF ablation with the CF catheter. The use of optimal CF (>10 g) was associated with higher success.

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References

CLINICAL PERSPECTIVE

A major advancement in the field of atrial fibrillation ablation has been the advent of radiofrequency ablation catheters with the capability of sensing the contact force (CF) between the catheter tip and tissue. It would stand to reason that knowledge of CF would allow more optimal lesion delivery during atrial fibrillation ablation and improve procedural efficacy. Here, we report the results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) trial, a multicenter, prospective trial that randomized 300 patients with paroxysmal atrial fibrillation to ablation with a CF-sensing catheter or to a standard radiofrequency ablation catheter in the control group. Primary effectiveness at 12 months was 67.8% in the CF group and 69.4% in the control group (P=0.0073 for noninferiority), which met criteria for noninferiority, and safety was not different between the groups. These results are not surprising, given that operators were not given CF guidelines for ablation. During this trial, CF guidelines based on results from other concurrent studies become available, prompting a retrospective analysis of the data. When the CF group was divided into an optimal group (≥90% ablations with ≥10 g) and a nonoptimal group, primary effectiveness was 75.9% versus 58.1% (P=0.018), respectively. These results demonstrate the clear benefit of good contact between catheter and tissue during atrial fibrillation ablation, which may improve procedural efficacy.
Randomized, Controlled Trial of the Safety and Effectiveness of a Contact Force–Sensing Irrigated Catheter for Ablation of Paroxysmal Atrial Fibrillation: Results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) Study

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카테터의 접촉력을 감지하는 시스템은 심방세동 절제술에 유용하다: TOCCASTAR 연구

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초록

배경
 접촉력(contact force, CF)은 도자질제술의 병변 크기와 경백성의 주요 결정 인자로, 심방세동 절제술의 효율을 향상시킬 수 있는 임상적 기여를 갖고 있다. 본 연구의 목적은 방식성심방세동 환자의 치료에서 실시간으로 접촉력을 측정할 수 있는 새로운 관주(irrigated) 고주파 절제술 카테터의 안전성과 유효성을 평가하기 위함이다.

방법 및 결과
 총 300명의 증상이 있으며 약제에 내성인 발작성심방세동 환자들이 진단적, 다기관, 무작위 대조군 시험에 동록되었으며, 새로운 접촉력 감지 카테터군(CF군)과 비접촉력 카테터군(대조군)으로 무작위 배정되었다. 일차 유효성 종료점은 모든 폐종맥의 금성 전기적 고립 및 12개월째에 모든 향부정맥제를 종단한 후에도 증상을 동반한 심방부정맥의 재발이 없는 경우로 하였 다. 일차 안전성 종료점은 기기와 관련된 중증 부작용으로 하였 다. 종료점들은 비열등성을 보여주도록 디자인되었다. 양 군에서 모든 폐종맥을 고려시켰다. 유효성은 CF군 및 대조군에서 각각 75.9%와 58.1%였다(P=0.018). 일차 안전성 종료점에 해당하는 사건은 CF군과 대조군에서 각각 1.97%와 1.40% 발생하였다(절대차, 0.57%; 단층 95% CI의 최고값, 3.61%; 비열등성 P=0.0004).

결론
 접촉력 감지 절제 카테터는 일차 안전성 및 유효성 종료점을 만족시켰다. 또한, 적정 CF는 유효성을 향상시켰다.