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Direct or Coincidental Elimination of Stable Rotors or Focal Sources May Explain Successful Atrial Fibrillation Ablation

On-Treatment Analysis of the CONFIRM Trial (Conventional Ablation for AF With or Without Focal Impulse and Rotor Modulation)

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Objectives This study sought to determine whether ablation of recently described stable atrial fibrillation (AF) sources, either directly by Focal Impulse and Rotor Modulation (FIRM) or coincidentally when anatomic ablation passes through AF sources, may explain long-term freedom from AF.

Background It is unclear why conventional anatomic AF ablation can be effective in some patients yet ineffective in others with similar profiles.

Methods The CONFIRM (Conventional Ablation for AF With or Without Focal Impulse and Rotor Modulation) trial prospectively revealed stable AF rotors or focal sources in 98 of 101 subjects with AF at 107 consecutive ablation cases. In 1:2 fashion, subjects received targeted source ablation (FIRM) followed by conventional ablation, or conventional ablation alone. We determined whether ablation lesions on electroanatomic maps passed through AF sources on FIRM maps.

Results Subjects who completed follow-up ($n = 94$; 71.2% with persistent AF) showed 2.3 ± 1.1 concurrent AF rotors or focal sources that lay near pulmonary veins (22.8%), left atrial roof (16.0%), and elsewhere in the left (28.2%) and right (33.0%) atria. AF sources were ablated directly in 100% of FIRM cases and coincidentally (e.g., left atrial roof) in 45% of conventional cases ($p < 0.05$). During a median (interquartile range) of 273 days (138 to 636 days) after one procedure, AF was absent in 80.3% of patients if sources were ablated but in only 18.2% of patients if sources were missed ($p < 0.001$). Freedom from AF was highest if all sources were ablated, intermediate if some sources were ablated, and lowest if no sources were ablated ($p < 0.001$).

Conclusions Elimination of stable AF rotors and focal sources may explain freedom from AF after diverse approaches to ablation. Patient-specific AF source distributions are consistent with the reported success of specific anatomic lesion sets and of widespread ablation. These results support targeting AF sources to reduce unnecessary ablation, and motivate studies on FIRM-only ablation. (The Dynamics of Human Atrial Fibrillation; NCT01008722) (J Am Coll Cardiol 2013;62:138–47) © 2013 by the American College of Cardiology Foundation

Atrial fibrillation (AF) is a major cause of morbidity and mortality, for which pharmacologic approaches for rate (1) or rhythm control (2) remain suboptimal. Catheter ablation is a

See page 148

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nonpharmacological therapy with the potential to eliminate AF, yet although it is more effective than medications (3–5), it has had suboptimal success for paroxysmal (6) and persistent (7,8) AF.

Mechanistic uncertainty for AF may contribute to these limitations of ablation. When mechanisms are well defined, such as for Wolff-Parkinson-White syndrome (9) or atrioventricular nodal reentry (10), ablation provides >85% to 90% one-procedure success. Conversely, the reentry circuits or focal sources that sustain AF are undefined after AF has been triggered by ectopy (from pulmonary veins [PVs] or elsewhere). It is thus unexplained how paroxysmal or persistent AF may be eliminated by ablation that does (5–7,11), but also does not (12–14), isolate the PVs.

We hypothesized that freedom from AF should be higher if lesions pass through stable rotors or focal sources, mechanisms recently shown to sustain AF in the CONFIRM (Conventional Ablation With or Without Focal Impulse and Rotor Modulation) trial (15) and independent reports (16,17) than if they do not. These studies used a novel computational approach to map stable sources in >97% of patients with paroxysmal or persistent AF, in whom source ablation (FIRM) improved AF freedom compared with conventional ablation alone on intention-to-treat analysis (15). However, although sources were seen in patients in both limbs of CONFIRM, it is unclear whether conventional ablation was more successful if passed through, rather than bypassed, AF sources.

We tested our hypothesis by defining the locations of ablation lesions and AF sources in each patient in each limb of the CONFIRM trial (FIRM-guided and -blinded). We determined whether lesions that passed through AF sources, directly by FIRM-mapping guidance or coincidentally by conventional anatomic ablation, conferred higher long-term freedom from AF in a pre-specified on-treatment analysis of the CONFIRM trial.

Methods

Study design and enrollment. CONFIRM (15) prospectively enrolled 92 subjects at 107 consecutive AF ablation procedures for standard-of-care indications. Subjects were ≥21 years of age with AF despite receiving one or more Class I or III anti-arrhythmic drugs. To study AF sources and their response to ablation across a broad spectrum of AF presentations, we included patients with paroxysmal, persistent, and longstanding persistent AF (8) and AF despite prior conventional ablation. The only exclusion criterion was an inability or refusal to provide specific written informed consent.

Consecutive cases were prospectively mapped and assigned in a 2:1 ratio to FIRM-blinded (conventional) ablation alone or, after real-time FIRM mapping had been developed, to FIRM-guided ablation comprising targeted source ablation (FIRM) followed by conventional ablation.

Abbreviations and Acronyms

AF = atrial fibrillation
ECG = electrocardiography
FIRM = focal impulse and rotor modulation
LA = left atrium
PV = pulmonary vein
RA = right atrium
WACA = wide-area circumferential ablation

Electrophysiology study. Electrophysiology study was performed after patients discontinued antiarrhythmic medications for 5 half-lives (for amiodarone: >60 days [median: 230 days]) (Table 1). Intravenous heparin was infused to maintain an activated clotting time >350 s. A 64-pole basket catheter (48- or 60-mm diameter; 4 to 6-mm electrode spacing; Constellation, Boston Scientific, Natick, Massachusetts) was advanced trans-septally to map the left atrium in all patients and to map the right atrium in 73 patients (including all FIRM-guided cases).

Figure 1A shows a patient in whom simultaneous biatrial baskets were used (recent studies have used one basket for both atria [16,17]). AF was observed in 101 cases (including FIRM-guided cases) (15). When required, AF was induced (rapid pacing: n = 26; isoproterenol: n = 2) because several studies have shown similar frequency (18) and spatial activation (19) for induced versus spontaneous AF. Unipolar and bipolar AF electrograms were filtered at 0.05 to 500 Hz and exported at 1-kHz sampling frequency.

FIRM mapping of AF sources. FIRM mapping for AF has been described previously (15,19). Briefly, AF electrograms were recorded in a wide field of view and analyzed using RhythmView (Topera, San Diego, California) to produce maps of AF propagation. Figure 1B shows a FIRM map of an AF rotor (i.e., red-to-blue, early-meets-late spiral wave). As shown in Figure 1C, this rotor lay at a lateral right atrial site that would not be ablated conventionally.

AF propagation (FIRM) maps were analyzed intraprocedurally in FIRM-guided patients to guide ablation, and post-procedurally in FIRM-blinded patients. *Electrical rotors* (Figs. 1B and 2) were defined as sustained clockwise or counterclockwise activation around a center of rotation, and *focal impulses* (Fig. 2) were defined by centrifugal activation from an origin. Rotors and focal impulses were considered AF sources only if stable in repeated samples over 30 to 120 min (i.e., thousands of cycles), distinct from transient fibrillatory activity (20,21). The AF focal source origin or rotor center of rotation was located by its electrode coordinates and "shadowed" digitally within each patient-specific anatomic shell (NavX, St. Jude Medical, Inc., St. Paul, Minnesota) at the time of each FIRM map to eliminate errors from subsequent possible movement. Each digital shell was created, in turn, using careful sampling of atrial and venous points with reference to (or fused with) pre-procedural patient-specific computed tomographic scans when available.

Ablation approach. Radiofrequency energy was delivered with a 3.5-mm tip irrigated catheter (Thermocool, Biosense-Webster, Diamond Bar, California) at 25 to 35 W or, in heart failure subjects, an 8-mm tip catheter (Blazer,