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EDITORIAL COMMENT

Pulmonary Vein Isolation With a Pace Capture–Guided Approach

Durable or Debatable?*

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Pulmonary vein (PV) isolation (PVI) is the foundation of effective catheter ablation for atrial fibrillation (AF). Data from randomized trials demonstrate that PVI leads to a 15-fold greater maintenance of sinus rhythm in patients with paroxysmal AF at 1 year compared with antiarrhythmic drug therapy (1). Moreover, PVI is associated with significant decreases in cardiovascular hospitalization and improved quality of life (1,2). Although PVI is the most critical endpoint of AF ablation, achieving durable isolation remains one of the greatest limitations of our current ablation procedure (3).

Maintenance of sinus rhythm in long-term follow-up after PVI remains disappointingly low. Although there are several reasons for AF recurrence after catheter ablation, including disease progression, lack of durable PVI after ablation is a significant contributor (3). Despite excellent acute PVI success rates, recurrent PV conduction is present in 70% of patients at 3 months (4). PV reconnection, although observed in many patients without AF recurrence, is associated with a 40% higher rate of AF recurrence (3).

Given the high rates of PV reconnection following ablation, clinicians have used a variety of measures to improve the durability of PVI beyond testing for entrance and exit block. These adjunctive techniques are well known and include monitoring for recurrent PV conduction for 20 to 30 min postablation, adenosine administration to provoke dormant conduction, and, more recently, the use of contact-force sensing catheters. By and large, the evidence supporting most of these adjunctive techniques is mixed, and current guidelines reflect this uncertainty, with most techniques being supported by Class IIB recommendations (5).

Another adjunctive technique to improve durability of PVI with variable evidence is the pace-guided approach. In this technique, after circumferential PVI, high-output pacing (10 mA at 2 ms) is applied along the ablation line. Sites with left atrial capture are ablated further until loss of capture (unexcitability) is achieved. Data from animal models suggest that loss of capture at ablation sites is associated with more uniform and transmural lesions (6). Early observational data with a pace-guided approach demonstrated that sites of pace capture were very common (92 of 112 circumferential ablation lines) and that ablation to unexcitability at these sites was associated with 79% freedom from atrial arrhythmia at 1 year (7). A subsequent randomized clinical trial conducted at 2 centers compared conventional PVI with pace-guided PVI demonstrated improved freedom from AF or tachycardia (AT/AF) at 1 year (83% vs. 52%, $p < 0.001$) after a single procedure (8). Despite this promising observational data from several investigators and optimistic short-term outcomes, there are few to no data on the long-term outcomes following PVI guided by loss of pace capture on the ablation line.

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In this issue of *JACC: Clinical Electrophysiology*, Moser et al. present long-term follow-up data out to 5 years (9) from a single-center subset of their original randomized clinical trial (8). The authors analyzed 74 patients of the original 103 patients enrolled with drug-refractory paroxysmal AF (those enrolled at the University Heart Center Hamburg). As might be expected, the pace-guided group had longer procedure times (157 min vs. 109 min, $p < 0.0001$) but similar fluoroscopy times (24 min vs. 23 min, $p = 0.21$).

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Surprisingly, after achievement of unexcitability in the pace-guided group, only 12 of 38 patients had evidence of right- and left-sided circumferential isolation; the remaining 26 patients required ablation of conduction gaps with guidance of a circular catheter. At 1 year, freedom from AT/AF after a single procedure was greater in the pace-guided group (80% vs. 49%); this superiority was maintained at a mean follow-up of 5.25 ± 1.0 years (71% vs. 26%, $p = 0.0016$). In follow-up, patients in the pace-guided group had fewer repeat procedures (mean: 1.97 vs. 1.06, $p < 0.0003$). Even in the pace-guided group, however, PV reconnection was common among patients with AF recurrence requiring a second procedure (15 of 36, 43%). On the basis of the lower rates of recurrent AT/AF in the pace-guided group, the authors hypothesized that pace-guided PVI results in more durable lesion formation and PVI. Moser et al. should be congratulated for not only conducting a randomized trial to determine the efficacy of pace-guided PVI but also for reporting long-term outcomes, a challenge and opportunity that is frequently lost. Such long-term results from randomized trials provide critically important guidance for clinical practice.

Although the long-term results reported by Moser et al. (9) suggest superiority of a pace-guided approach, there are several study limitations that should be kept in mind. First, the present analysis of long-term outcomes includes subjects enrolled at 1 of 2 centers only. As the authors acknowledge, the exclusion of 23 patients from the original cohort and analysis of data from a single center may bias the results. Second, the trial, although randomized, included a relatively small number of patients. It is possible that the findings could be due to chance and represent type I error. Third, the postablation monitoring was limited, potentially as infrequent as once per year after the initial 12 months. With more intensive monitoring, the recurrence rates would likely have been higher, and the observed difference between the pace-guided and conventional arms may have been less dramatic.

Consistent with observations from animal models, the authors hypothesized that improved outcomes in the pace-guided group were due to more durable transmural lesions and PVI; however, not all of the results support this hypothesis. Notably, PV reconnection rates did not differ in those patients who underwent repeat ablation (43% vs. 47% of veins). Although a difference was observed at second repeat ablations, one would expect more durable lesion formation to result in less PV reconnection immediately after ablation, even in those with recurrence requiring repeat ablation. Moreover, after achieving loss of capture along the ablation line in the pace-guided group, a significant number of patients (26 of 38) continued to have evidence of PV conduction. These findings raise several questions. Were the initial pace-guided lesions sets noncontiguous and thus insufficient without additional circular mapping catheter-guided ablation? Is ablating to unexcitability doing something other than increasing the durability of PVI? Is it influencing triggers or substrate through other mechanisms?

Prior work has shown that loss of capture identifies sites that are distinct from sites of dormant conduction identified with adenosine testing. Kogawa et al. found that after PVI, dormant PV conduction was identified after adenosine in 16% of PVs, whereas pace capture was identified in 33% of veins (10). Furthermore, only 12% of veins exhibited both dormant PV conduction and pace capture. In a parallel cohort study comparing a pace capture-guided versus an adenosine-guided approach to PVI, in the subset of patients who underwent both maneuvers, 24% of patients still had evidence of dormant conduction after loss of pace capture was confirmed (11). These findings demonstrate that pace-capture and dormant conduction are either 1) imperfect methods of identifying incomplete PVI or 2) identify different mechanisms of reconnection.

It is possible that ablation until loss of pace-capture ablates a larger volume of antral (and atrial) tissue; this additional debulking may be responsible for elimination of additional triggers, perhaps rotors or autonomic ganglia, for instance, and improved efficacy. This might also explain the dramatically better results with pace-guided ablation even though PV reconnection rates at first repeat ablation were similar to those who underwent a standard ablation.

Given the notable increase in efficacy observed with the pace-guided approach in this trial, should

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clinicians incorporate this technique into their practice? Although the data are promising, several features of the current study and aggregate evidence invite caution. The 5-year freedom from AT/AF in the pace-guided ablation arm after a single procedure with a noncontact force sensing catheter was 71%. This seems overly optimistic given the results across both clinical trials and observational studies of catheter ablation for paroxysmal AF. Estimates from meta-analysis suggest that the average freedom from AT/AF after a single procedure in long-term follow-up is 54% (95% confidence interval: 44% to 63%) in patients with paroxysmal AF (12).

Given that this study predates the advent of contact force-sensing catheters, it is not clear what the impact of a pace-guided approach might be in contemporary practice with contact force-guided ablation. Moreover, it is unknown whether pace-guided ablation provides incremental, inferior, or equivalent benefit to adenosine-guided PVI. The limited available observational data suggest that outcomes are comparable with each approach (11). Given all of these uncertainties, a clinical trial comparing an adenosine-guided approach with a pace-guided approach or both together (all with a 20-min monitoring period) is needed. It is also possible, and perhaps likely, that a patient-specific approach based on pre-procedural imaging, intraprocedural imaging, or electroanatomic substrate characterization may help guide selection of adjunctive techniques to ensure durable PVI. For example, thicker atrial tissue at the left atrial-PV junction, sites of limited impedance drop, or use of acoustic radiation force imaging might indicate higher risk anatomy that could from both pace- and adenosine-guided PVI (13,14).

The quest for more durable and effective PVI will continue. The long-term results with pace-guided PVI offer promise but also raise many questions. Time will tell if a pace-guided approach to PVI is durable or debatable.

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