Comparing Different Strategies for Catheter Ablation of Atrial Fibrillation

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To doubt everything or to believe everything are two equally convenient options; both dispense with the necessity of reflection. —Jules Henry Poincaré

Opportunities for progress in clinical medicine often follow contradiction of previously accepted data. The impact of the first study comparing circumferential pulmonary vein (PV) ablation (left atrial catheter ablation) and segmental PV isolation was sweeping. The finding by Oral and colleagues that left atrial ablation improved outcomes over PV isolation in patients with paroxysmal atrial fibrillation (AF)1 was immediately accepted. This acceptance was based on the respect due these investigators, as well as on the consistency of these results with those reported using the separate techniques via different programs; previous reports of circumferential PV ablation2 and PV isolation3 estimated single-procedure success rates of 85% and 56%, respectively, in patients with mostly paroxysmal AF. Many practitioners “waiting in the wings” were convinced to begin AF ablation programs using the left atrial ablation technique on the basis of this information. This reaction was reinforced because most viewed this technique as easier, requiring a single transseptal puncture and avoiding the complexities of interpreting PV electrogram end points.

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The study by Karch and coworkers, presented in this issue of Circulation, takes on even greater importance when viewed through this perspective.4 The authors compared circumferential PV ablation and segmental PV vein isolation in 100 patients with frequent, drug-refractory, and mostly (89%) paroxysmal AF. Their hypothesis, in line with conventional wisdom, was that circumferential ablation would reduce the relative risk of recurrent AF by 66% as compared with PV isolation. The authors held to the conceptual standards developed by the respective founders of each technique.2,3 Circumferential ablation was guided by electroanatomic mapping using separate right and left PV circles, 5 mm from the ostia as defined by angiography, and a mitral “isthmus” line; the posterior wall linear lesion was not performed because of concern about esophageal injury. Radiofrequency energy was delivered with an 8-mm-tip (55°C, 50 to 70 W) or an irrigated (48°C, 35 to 50 W) catheter, based on electrogram reduction. No electrophysiological assessment of PV or isthmus block was performed. PV isolation was guided by circular multielectrode catheter recordings that used entrance block findings. Ablation was performed with a 4-mm-tip catheter (48°C, 30 to 35 W). The primary end point was freedom from atrial tachyarrhythmias (>30 seconds) based on a 7-day Holter monitor performed at 6 months in patients who were not treated with antiarrhythmic drugs. Secondary end points were freedom from arrhythmia symptoms (>1 month after ablation) and a composite of laboratory complications (cardiac tamponade, thromboembolic complications, PV stenosis).

Karch and coworkers observed that patients treated with segmental PV isolation fared better than did those with circumferential ablation. More patients were free of atrial arrhythmias on Holter monitoring at 6 months (66% versus 42%, P=0.02) and free of arrhythmia symptoms (82% versus 54%, P<0.01). The vital importance of monitoring was emphasized by the finding that many patients (8 of 29 in the circumferential group, 8 of 17 in the segmental group) with documented AF recurrence were asymptomatic. Atypical flutter contributed significantly to recurrence, particularly in the circumferential group (9 of 29 patients with recurrent arrhythmias). Repeat procedures (3 to 6 months after the initial procedure) were performed in 12 patients with circumferential ablation and 8 patients with a segmental approach; 10 of these patients were free of arrhythmias at 6 months and were included in the primary end point determination. Complications occurred in 12% of the circumferential group and 14% of the segmental group, which is compatible with previous reports, except for the astonishing absence of thromboembolic complications in previous series of left atrial substrate ablation.1,2,5 PV stenosis (>50% by CT imaging at 3 months) did not result in symptoms and occurred in both groups, but it was more frequent with segmental isolation. Notable but not included in this safety end point was the observation of pericardial effusion that did not require treatment in 22 patients with circumferential ablation as compared with 5 patients with segmental ablation.

The authors began the attempt to elevate the discussion above the level of “whose procedure is superior” by careful consideration of why their results may differ from those reported previously. Their results are most notably different from those of Oral and coworkers1 in the outcome of patients treated with circumferential PV ablation (primary end point success 42% in the present study, 88% in the previous). The difference in end points in the 2 studies accounts for at least

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some of this apparent discrepancy. The study by Oral et al used freedom from symptomatic AF at 6 months as a primary end point. To be fair, this end point governed the results of all of the series of AF ablation at the time the Oral et al study was published, apparently fueled by the belief that patients with highly symptomatic AF episodes could not possibly have asymptomatic episodes either before or after ablation. The evidence to the contrary in this and other treatment settings has been explored previously.\textsuperscript{6,7} Perhaps the single most compelling finding in the Karch and coworkers study is the incidence of asymptomatic arrhythmia recurrence demonstrated by extensive monitoring. This observation is even more critical when examining the results of studies from referral centers because the investigators may not be primarily responsible for the routine follow-up of patients after they leave the electrophysiology laboratory.

Other factors considered by the authors to explain the difference with the Oral et al study include the absence of a posterior linear lesion in their series, the more frequent inclusion of patients with structural heart disease, and the different accounting of atypical atrial flutter. The posterior lesion has been abandoned by many clinicians because of concern over esophageal-atrial fistula; however, it appears from published reports\textsuperscript{8} as well as from preliminary data provided by intracardiac echocardiographic imaging\textsuperscript{9} that the esophagus often approaches the atrium close to the pulmonary veins (thus approachable with ostial ablation with either technique), rather than at the posterior atrial wall. In my opinion, avoidance of esophageal injury depends more on imaging (intracardiac echocardiography, digital image fusion) than ablation strategy. Moreover, a recent report by Pappone and coworkers asserts that the addition of 2 posterior lines to circumferential PV ablation reduced the incidence of atypical atrial flutter, without an effect on freedom from AF recurrence.\textsuperscript{5} Left atrial flutter has been estimated to recur in 2.5% to 20% of patients after left atrial substrate ablation; some episodes are apparently self-limited. Atypical atrial flutter occurred in only 1 patient after left atrial ablation in the Oral et al study, but was more frequent in the Karch et al study, occurring in 9 patients after circumferential ablation and in 1 patient after PV isolation.

There are several other factors, not considered by the authors, that continue to confound direct comparisons between series. Recurrence of AF, although seemingly a dichotomous variable, can be difficult to codify in real life. There is near-universal acceptance of the idea that early recurrence does not necessarily predict late failure. After this 4- to 6-week period, however, different styles of reporting abound (on/off antiarrhythmic drugs, symptomatic versus monitored recurrence, freedom from atrial tachyarrhythmias versus 90% reduction in episodes). Potentially even more difficult are the different "styles" of patient recurrence, the time-dependent nature of which defies adequate description in a "snapshot" summary. Some patients have rare AF episodes within the first months of ablation, but are free of recurrence when not taking medication after longer-term follow-up. Alternatively, patients free of AF recurrence for periods of time can have isolated episodes of AF under the duress of systemic illness or surgery. To the purist, both situations are ablation failures, but this obscures the obvious difference between patients who are not helped by the index procedure at all (true failure). All of these potentially confounding influences argue for universal reporting criteria that primarily measure objective criteria under ordinary conditions at a fixed, distant point from an index procedure.

To this same end, the 2 different techniques often are unfairly compared by relatively artificial constructs. Because of concern about PV stenosis, segmental PV isolation often is performed with 4-mm-tip catheters at relatively low power settings, whereas circumferential ablation is performed with 8-mm-tip or irrigated catheters at higher outputs. Previous studies showed that increased power delivery significantly affects the success of segmental isolation procedures.\textsuperscript{10} On the other side, segmental isolation is performed with an electrophysiological end point, and circumferential ablation is not. Although the mechanism of efficacy of both procedures is less than completely clear, it is strange and unprecedented to expect that less electrophysiological investigation will triumph over more. As should be obvious, progress in the development of future improvements in ablation strategies will be made only if proper comparisons and precise measurements are made.

As a point of departure, I would like to propose universal reporting criteria for scientific studies of AF ablation. These will be more rigorous than could be tolerated under typical clinical practice settings, but they will be essential to future observations and comparisons. Strict, objective, and standard definitions of paroxysmal, persistent, and permanent AF should be respected. There may well be important differences in the response to various ablation strategies in these markedly different AF pathophysiologies that will otherwise remain clouded in semantics. Patient-reported symptoms are important after ablation procedures, and every attempt should be made to document the cause of suspicious symptoms with electrocardiographic recordings. The absence of symptoms should not be assumed to be equivalent to a "cure" of AF, however. Furthermore, quality-of-life improvement after ablation, an essential metric of success, was observed to be more independent of outcome than was expected.\textsuperscript{11} Primary end points should be determined on the basis of objective measures such as long-term, continuous ECG recordings, with reporting mechanisms that do not depend on patient-triggered events, performed 6 months after the procedure (to intentionally miss some self-limited early arrhythmias). All atrial arrhythmias should be included in the data, as left atrial tachycardia/flutter after ablation is a clinically and mechanistically significant end point. Results in patients no longer taking antiarrhythmic medications should be held as the reference standard. Eventually, ultra-long-term follow-up studies to address the effect of ablation of focal AF on the development of senescent AF will be necessary to address whether actual cure of AF is feasible.

The authors are to be congratulated for such an important contribution, not only to our present knowledge but also to the conduct of further investigation. Such careful investigations are exceptionally difficult, particularly with the overwhelming volume of monitoring data to manage. Continued
progress in the development of an optimal ablation strategy for AF will require nothing less.

References


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