

## AF Termination: the Holy Grail of Persistent AF Ablation?

Dennis H. Lau, MBBS; Anthony G. Brooks, PhD; Prashanthan Sanders, MBBS, PhD

Cardiovascular Research Centre, Department of Cardiology, Royal Adelaide Hospital and the Disciplines of Medicine and Physiology, University of Adelaide, Adelaide, Australia

### Introduction

The optimal catheter ablation approach for long-standing persistent atrial fibrillation (AF) remains elusive despite significant advances made in our understanding of this arrhythmia. A recent systematic review highlighted the significant variation in procedural success rate both within and between techniques, necessitating repeat ablation procedures and anti-arrhythmic drugs to achieve improved outcomes in those with long-standing persistent AF.<sup>1</sup> Indeed, current expert consensus statement recommended ablation beyond ostial pulmonary vein isolation for these patients.<sup>2</sup> Despite incorporating various substrate modification techniques which commonly include linear lesions and targeting of complex fractionated electrograms, the reported success rates from various laboratories are still below par to those in paroxysmal AF patients.<sup>1</sup> Perhaps the often dilated and chronically remodeled atria in longstanding persistent AF patients harbor complex structural substrates capable of maintaining the arrhythmia beyond amelioration even with extensive catheter ablation in some. Certainly, this reflects our incomplete understanding of the complex mechanisms underlying this arrhythmia.

Regardless of the approach, electrophysiologists

must be clear of the endpoints for their chosen ablation strategy. Pulmonary vein ablation remains the cornerstone in most catheter ablation strategies with complete electrical isolation accepted as its goal and if linear lesions are attempted, completeness of lesion sets should be confirmed using activation mapping with appropriate pacing maneuvers.<sup>2</sup> Endpoints for electrogram guided ablation are less well defined but can include elimination of fractionated signals or transformation into discrete electrograms, and slowing or organization of local fibrillatory cycle length.<sup>3</sup> Apart from the above-mentioned electrophysiological endpoints, termination of AF to sinus rhythm or atrial tachycardia has been pursued as procedural endpoint with the stepwise ablation approach. Laboratories using this approach reported high long term success rate in up to 88% without anti-arrhythmic drugs despite the need for multiple procedures due to recurrent atrial tachycardias.<sup>3-6</sup> Specifically, from a prospective study of 153 consecutive patients, O'Neill and co-workers demonstrated that 95% of those with AF termination remained in sinus rhythm at a mean follow-up duration of 32 months as compared to just 52% in those without AF termination following repeat ablation procedures.<sup>6</sup> Likewise, in a smaller series of 88 patients by Rostock et al the overall success rate was 95% in those with as compared to 5% in those without termination of

**Corresponding Address :** Prashanthan Sanders, Cardiovascular Research Centre, Cardiovascular Investigation Unit, Royal Adelaide Hospital, Adelaide, SA 5000, AUSTRALIA.

AF in two procedures and a mean follow-up duration of 20 months.<sup>5</sup> Therefore, termination of AF appeared to be prognostically important in long-standing persistent AF.

In a recent study published in *Heart Rhythm* entitled "Atrial fibrillation termination as a procedural endpoint during ablation in long-standing persistent atrial fibrillation", Elayi and colleagues undertook a prospective multi-centre evaluation of the prognostic impact of AF termination during ablation in a large cohort of 306 patients over a mean follow-up period of 25 months.<sup>7</sup> The ablation strategy in this study consisted of pulmonary vein antrum isolation followed by complex fractionated atrial electrograms ablation. They achieved AF termination in 178 patients (58%) at the first procedure. In total, long term sinus rhythm maintenance off anti-arrhythmic drugs was not significantly different between those with (68%, 121/178) and without (70%, 90/128) AF termination at the first procedure. In addition, no difference was observed whether sinus rhythm or atrial tachycardia was achieved with AF termination during the initial ablation. AF recurrence was seen in 57/178 (32%) and 38/128 (30%) patients with and without initial AF termination: 46/57 (81%) and 28/38 (74%) of these patients underwent a second procedure whereby AF termination was again achieved in 26/46 (57%) and 15/28 (54%) respectively. Interestingly, long term success off anti-arrhythmic drugs after two procedures remained similar between those with (83%, 147/178) and without (82%, 105/128) AF termination. Further analysis showed that if AF was terminated into atrial tachycardia during ablation, those with focal atrial tachycardia had better longer term success than those with macro-reentrant atrial tachycardia (83 vs. 57%,  $p=0.026$ ).

The results presented by Elayi et al appear disparate to the experience of the Bordeaux and Hamburg laboratories. However, the following fundamental differences need to be considered: First, the study population differed amongst these three studies with a younger cohort in the O'Neill series and what appears to be shorter duration of AF in patients from the O'Neill and Rostock reports.

Second, the mean baseline AF cycle length in the Elayi series was shortest amongst the 3 studies at 128ms, perhaps implying more remodeled atria. Third, utilization of anti-arrhythmic drugs in the peri-procedural and follow-up periods was different with exclusively no amiodarone use in the Elayi series. Fourth, although all studies aimed to terminate AF during the procedure, different ablation strategy was employed with pulmonary vein antrum isolation followed by complex fractionated atrial electrograms ablation in the Elayi report and stepwise ablation approach in the other two. Last, post-procedural management strategy appears different with the Rostock series reporting use of DC cardioversion in the first 3 months for any arrhythmia recurrence.

Indeed, both the duration of continuous AF and baseline AF cycle length have been found to be predictive of maintenance of sinus rhythm by catheter ablation in a recent report.<sup>8</sup> Perhaps the more advanced underlying electrical and structural remodeling due to longer AF duration (> 2 years) in patients from the Elayi series portends a greater prognostic burden than achieving termination of AF during catheter ablation. This may in part account for their observations that atrial tachycardias of a focal mechanism had a better outcome than those of a re-entrant type given the complex atrial substrate in their patients as evidenced by their short baseline AF cycle length further alluding to their arrhythmia chronicity. Another recent report on the reversibility of atrial electrical and structural remodeling due to chronic atrial stretch following removal of the stretch stimulus highlighted that the substrate predisposing to AF might be reversed.<sup>9</sup> On this note, the lack of use of amiodarone and DC cardioversion in the Elayi series would have reduced the opportunity for reverse atrial remodeling thereby confounding the benefits of achieving AF termination following catheter ablation.

In summary, AF is a heterogeneous disease which requires a tailored management approach in the individual patient based on their predisposing risk profile and the nature and duration of their arrhythmia. Termination of AF during the stepwise

ablation approach in patients with shorter duration of AF and longer baseline AF cycle length together with aggressive post-procedural rhythm control has shown great promise as a prognostically important ablation endpoint. Taken together with the findings by Elayi et al, the termination of AF as a procedural endpoint may not be the Holy Grail during the ablation of long-standing persistent AF and will require further investigations.

## References

1. Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, Hsu LF, Sanders P. Outcomes of long-standing persistent atrial fibrillation ablation: A systematic review. *Heart Rhythm* 2010; In press, doi:10.1016/j.hrthm.2010.01.017.
2. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, Damiano RJ, Jr., Davies DW, Haines DE, Haissaguerre M, Iesaka Y, Jackman W, Jais P, Kottkamp H, Kuck KH, Lindsay BD, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Natale A, Pappone C, Prystowsky E, Raviele A, Ruskin JN, Shemin RJ. Hrs/ehra/ecas expert consensus statement on catheter and surgical ablation of atrial fibrillation: Recommendations for personnel, policy, procedures and follow-up. A report of the heart rhythm society (hrs) task force on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm* 2007; 4:816-861.
3. Takahashi Y, O'Neill MD, Hocini M, Dubois R, Matsuo S, Knecht S, Mahapatra S, Lim KT, Jais P, Jonsson A, Sacher F, Sanders P, Rostock T, Bordachar P, Clementy J, Klein GJ, Haissaguerre M. Characterization of electrograms associated with termination of chronic atrial fibrillation by catheter ablation. *J Am Coll Cardiol* 2008; 51:1003-1010.
4. Haissaguerre M, Hocini M, Sanders P, Sacher F, Rotter M, Takahashi Y, Rostock T, Hsu LF, Bordachar P, Reuter S, Roudaut R, Clementy J, Jais P. Catheter ablation of long-lasting persistent atrial fibrillation: Clinical outcome and mechanisms of subsequent arrhythmias. *J Cardiovasc Electrophysiol* 2005;16:1138-1147.
5. Rostock T, Steven D, Hoffmann B, Servatius H, Drewitz I, Sydow K, Mullerleile K, Ventura R, Wegscheider K, Meinertz T, Willems S. Chronic atrial fibrillation is a biatrial arrhythmia: Data from catheter ablation of chronic atrial fibrillation aiming arrhythmia termination using a sequential ablation approach. *Circ Arrhythm Electrophysiol* 2008; 1:344-353.
6. O'Neill MD, Wright M, Knecht S, Jais P, Hocini M, Takahashi Y, Jonsson A, Sacher F, Matsuo S, Lim KT, Arantes L, Derval N, Lellouche N, Nault I, Bordachar P, Clementy J, Haissaguerre M. Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint. *Eur Heart J* 2009; 30:1105-1112.
7. Elayi CS, Di Biase L, Barrett C, Ching CK, Aly MA, Lucciola M, Bai R, Horton R, Fahmy TS, Verma A, Khaykin Y, Shah J, Morales G, Hongo R, Hao S, Beheiry S, Arruda M, Schweikert RA, Cummings J, Burkhardt JD, Wang P, Al-Ahmad A, Cauchemez B, Gaita F, Natale A. Atrial fibrillation termination as a procedural endpoint during ablation in long-standing persistent atrial fibrillation. *Heart Rhythm* 2010; In press, doi:10.1016/j.hrthm.2010.01.038.
8. Matsuo S, Lellouche N, Wright M, Bevilacqua M, Knecht S, Nault I, Lim KT, Arantes L, O'Neill MD, Platonov PG, Carlson J, Sacher F, Hocini M, Jais P, Haissaguerre M. Clinical predictors of termination and clinical outcome of catheter ablation for persistent atrial fibrillation. *J Am Coll Cardiol* 2009; 54:788-795.
9. John B, Stiles MK, Kuklik P, Brooks AG, Chandy ST, Kalman JM, Sanders P. Reverse remodeling of the atria after treatment of chronic stretch in humans: Implications for the atrial fibrillation substrate. *J Am Coll Cardiol*; 55:1217-1226.