Circles and lines: are we opening the Pandora’s box of non-paroxysmal atrial fibrillation ablation?

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This editorial refers to ‘Prospective randomized comparison between a fixed ‘2C3L’ approach vs. stepwise approach for catheter ablation of persistent atrial fibrillation’ by J.-Z. Dong et al., on page 1798–1806.

Catheter ablation for rhythm control in patients with non-paroxysmal atrial fibrillation (AF) is challenging. The latest guidelines for AF management give a class Ila (Level of Evidence A) and class Iib (Level of Evidence B) recommendation for catheter ablation of persistent and long-standing persistent (LSP) AF, respectively. This arises from the poor success rates reported in several studies (45–60% after a single procedure) and an increased risk of complications when extensive radiofrequency ablation is attempted. Moreover, many studies in non-paroxysmal AF are observational, using different strategies with different procedural endpoints that are often subjective and reproducible only by expert operators. As a result, an important variation in success rates is observed and no consensus exists as to the optimal ablation strategy.

Isolation of the pulmonary veins (PVs) and their embryological sibling, the posterior wall (the so-called pulmonary vein antral isolation, PVAI) is an essential step, but to achieve long-term success it is important to take it further. The importance of extending the ablation to non-PV sites is related to the significant structural and electrophysiological changes that take place when AF persists, a process known as ‘atrial remodelling’. In addition to PVAI, ablation strategies in non-paroxysmal AF are primarily aimed at eliminating non-PV triggers or altering the substrate, the latter usually being achieved with linear lesions or ablation of complex fractionated atrial electrograms (CFAEs). Meta-analyses have shown that CFAEs ablation in addition to PVAI improves success rates compared with PVAI alone, and this is primarily due to the studies conducted on patients with non-paroxysmal AF. The benefit of linear ablation is less clear, with a single-procedure clinical success off antiarrhythmic drugs (AADs) ranging from 11 to 74%. This is mainly explainable by an high incidence of incomplete linear block with consequent proarrhythmia.

In this issue of Europace, Dong et al. propose a fixed strategy for non-paroxysmal AF patients, named ‘2C3L’, consisting of bilateral circumferential PVAI (2C) and three linear lesions (3L), across the mitral isthmus (MI), the left atrial roof and the cavo-tricuspid isthmus (CTI). They compared this fixed approach to a modified version of the ‘stepwise’ approach commonly applied in non-paroxysmal patients: after PVAI and linear ablation (the ‘2C3L’ strategy described above), CFAEs were sought and eliminated to achieve AF termination. After PVAI and linear block were confirmed, if AF or atrial tachycardia spontaneously occurred during the procedure, additional empirical superior vena cava isolation or mapping-guided ablation of the atrial tachycardia was respectively performed.

In this single-centre, non-inferiority controlled trial they randomized 146 patients with non-paroxysmal AF (76% male, age 55 ± 11 years, 60% LSP) to undergo first-time catheter ablation using either the ‘2C3L’ approach or a ‘stepwise’ approach. At 12 months after the procedure, the ‘2C3L’ approach proved to be non-inferior to the ‘stepwise’ approach when considering freedom from atrial tachyarrhythmia off AADs (67 vs. 60%, P = 0.394; 95% confidence interval for risk difference −8.7 to 22.4%). This result was confirmed also with longer follow-up (after 25 ± 5 months, 57.5 vs. 52.1% of patients remained in sinus rhythm; P = 0.494) and when considering repeat procedures (with 1.4 ± 0.6 procedures after 21 ± 7 months of follow-up, 84.9 vs. 80.8% of patients were free from atrial tachyarrhythmia; P = 0.604). As expected, compared with the ‘stepwise’ approach, the fixed ‘2C3L’ approach was faster, with statistically significant shorter procedural, fluoroscopy, and radiofrequency times (222 ± 42 vs. 263 ± 41 min, 41 ± 9 vs. 55 ± 8 min, and 107 ± 32 vs. 128 ± 32 min, respectively; P < 0.001).

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Thus, this study suggests that in relatively young non-paroxysmal AF patients undergoing first-time ablation, a fixed ablation strategy encompassing effective linear ablation in addition to PVAI eliminates the need of CFAEs ablation.

While it has been previously shown that adding linear lesions increases success at follow-up when compared with PVAI plus CFAEs ablation, this is the first study to expressly assess the additional benefit of CFAEs ablation to effective linear ablation and PVAI in non-paroxysmal AF patients. Complex fractionated atrial electrograms ablation is one of the main components of the ‘stepwise’ approach and it is often performed before linear ablation. There are two main limitations in CFAEs-based ablation strategies. First, CFAEs are identified by visual inspection, a highly subjective target for ablation that is time consuming and hardly reproducible. Moreover, CFAEs ablation uses AF termination as an acute procedural endpoint, and this appears not to predict success at follow-up.

How does linear ablation work? First, it is important for linear ablation to be effective, that is, to produce bidirectional block. In this study, acute success rate for linear ablation was relatively high (>90% for CTI and LA roof; >80% for MI). This could explain the apparent contradiction with the recently reported STAR AF 2 trial, in which neither CFAEs elimination nor linear ablation improved clinical efficacy compared with PVAI alone in persistent AF patients. Indeed, in the STAR AF 2 trial only 74% of the patients of the PVAI plus LINES group achieved bidirectional block.

But why does an effective linear ablation work? Lines aim to compartmentalize the left atrium (LA), trying to duplicate the results seen in the surgical Maze procedures. With this notion, it is questionable for the right-sided CTI ablation to have a role. Indeed, it has been repeatedly shown that in patients with typical atrial flutter with or without documented AF, an ablation strategy targeting only the CTI is not useful to achieve long-term prevention of arrhythmia recurrence, while PVAI appears sufficient to control both arrhythmias. On the other hand, left-sided lines are thought to work by compartmentalizing the LA, thus reducing the excitable myocardial mass and atrial re-entrants circuits. But, at the same time they target non-PV triggers: a wide circumferential PVAI coupled with a roof line can isolate the posterior wall, while the epicardial lesion often needed to complete a mitral line effectively debunks the CS. Identification and ablation of non-PV triggers is important, as it has been shown that they are more prevalent in the non-paroxysmal AF population. Ablation of documented AF triggers or empirical ablation of sites associated with non-PV triggers has been shown to improve the freedom from AF at follow-up when compared with PV isolation alone. Moreover, our group has previously shown that in patients presenting with perimital flutter after LSP AF ablation, an ablation strategy aiming to eliminate PV and non-PV triggers is superior to MI block.

Thus, while it is important to move towards a unified approach, with objective endpoints that can pass the strict scrutiny of randomized clinical trials, the search for the optimal strategy to a life without non-paroxysmal AF should continue.

References