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BCS Editorial

Atrial fibrillation: time to personalise the ablation approach?

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Take Home Messages

- The variable success rate of pulmonary vein isolation (PVI) in the treatment of persistent atrial fibrillation (AF) has prompted the development of ablation strategies targeted outside the pulmonary veins.
- The DECAAF II study examined the hypothesis that PVI+fibrosis guided ablation during the first procedure, would improve freedom from arrhythmia compared with PVI alone for persistent AF.
- The study found no significant differences in atrial arrhythmia recurrence amongst patients treated with PVI+fibrosis guided ablation versus PVI alone.
- This study presented an important negative finding and further supports the use of PVI alone as the first-line strategy in persistent AF patients.
- Further studies are warranted to delineate the role of fibrosis-guided ablation in selected cases. Advances in computational modeling studies offer the potential to deliver personalised therapy for AF patients.

Introduction

The importance of pulmonary vein ectopy in the initiation and maintenance of atrial fibrillation (AF) is well recognised (1) resulting in pulmonary vein isolation (PVI) forming a key component of AF ablation procedures. The success rates of PVI alone are variable, and it has been observed that persistent AF ablation success rates (40-70%) are lower than paroxysmal AF success rates (60-70%) (2). The variability in reported outcomes may reflect variation in definitions of success, intensity of monitoring and the impact of non-pulmonary vein triggers or substrates for AF. Numerous strategies comprising substrate ablation beyond PVI have been investigated with variable degrees of success (3) iterating the requirement for better, more targeted ablation approaches. This editorial discusses the Determinant of Successful Radiofrequency Catheter Ablation of Atrial Fibrillation (DECAAF) II trial which aimed to assess the impact of PVI plus MRI-guided atrial fibrosis ablation versus PVI alone in persistent AF.

Atrial fibrosis

Atrial fibrosis is recognised as a key pathophysiological contributor to the development and maintenance of AF (4). The extent of atrial fibrosis can be investigated using advanced analysis of Late Gadolinium Enhancement-Magnetic Resonance Imaging (LGE-MRI) (5,6) (**Figure 1**). The importance of atrial fibrosis as a prognostic marker has been demonstrated by the original DECAAF study which revealed an independent association between atrial tissue fibrosis and an increased likelihood of recurrent arrhythmia in both

About the author

Neil Bodagh graduated with Honours and Distinction in Medicine from the University of Manchester in 2015. He started speciality training in 2020 as a Cardiology Academic Clinical Fellow in the South Thames deanery. He has come out of programme to commence a role as a Clinical Research Fellow in the Arrhythmia and Electrophysiology Research Group at King's College London/St Thomas' Hospital.

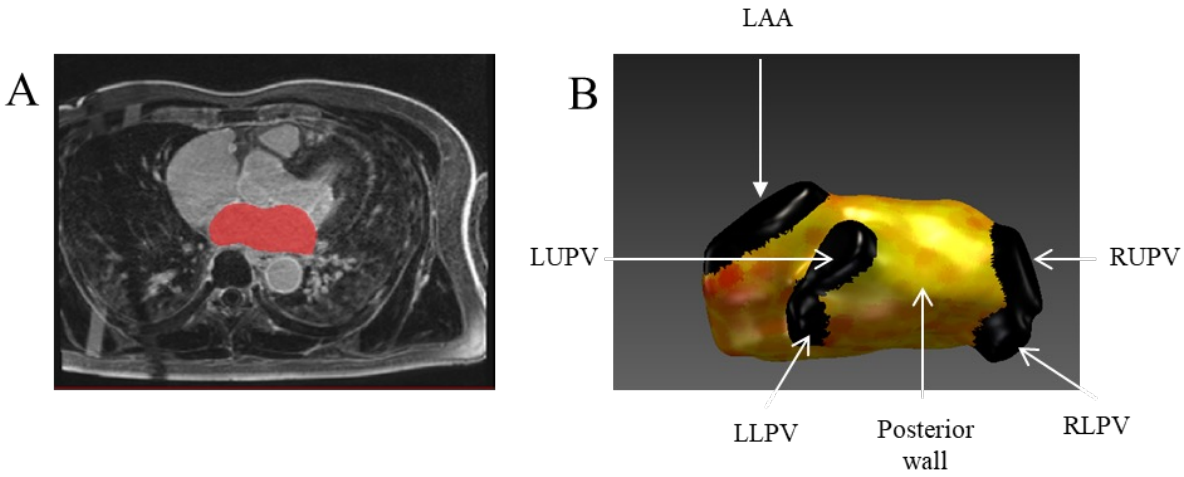

Figure 1. *Atrial fibrosis assessment using advanced analysis of late gadolinium enhancement-magnetic resonance imaging. (A) Left atrial segmentation from an atrial cardiac magnetic resonance imaging scan. (B) Left atrial fibrosis map. Red areas represent areas of detected late gadolinium enhancement. Areas in black indicate clipped LAA (left atrial appendage), LUPV (left upper pulmonary vein), LLPV (left lower pulmonary vein), RUPV (right upper pulmonary vein), RLPV (right lower pulmonary vein).*
Images created by Neil Bodagh using CEMRG software (cemrg.com).

paroxysmal and persistent AF patients undergoing catheter ablation (7). These observations resulted in the hypothesis that ablation targeting areas of atrial fibrosis detected on LGE-MRI in addition to PVI, may decrease atrial arrhythmia recurrence compared with PVI alone in persistent AF. This hypothesis was examined in the DECAAF II trial (8).

DECAAF II trial

The DECAAF II trial was a multicentre, randomised clinical trial comprising 843 patients with symptomatic or asymptomatic persistent AF undergoing first-time catheter ablation. Patients were assigned to PVI plus MRI-guided atrial fibrosis ablation or PVI alone. The primary endpoint was time to first atrial arrhythmia recurrence after a 3-month blanking period. The primary safety outcome was the occurrence of 1 or more of the following events within 30 days after the ablation procedure: stroke, pulmonary vein stenosis, bleeding, heart failure or death.

The study found that there was no significant difference in atrial arrhythmia recurrence between groups (PVI plus fibrosis-guided ablation [43.0%] versus PVI only [46.1%], hazard ratio 0.95 [95% confidence interval 0.77-1.17]). The study also found that patients in the fibrosis-guided ablation plus PVI group had a higher rate of the primary safety outcome (9 [2.2%] versus 0; p=0.001), with most of these complications being strokes. The authors concluded that MRI-guided fibrosis ablation plus PVI resulted in no significant difference in atrial arrhythmia recurrence.

Analysis

The authors are to be commended for their work. The study explored the hypothesis that PVI plus fibrosis-guided ablation could improve outcomes following catheter ablation for persistent AF. The authors presented an important negative study and proposed potential explanations for why the fibrosis-guided ablation approach failed to demonstrate benefit. It was discussed that the mechanisms by which fibrosis may lead to the initiation and/or perpetuation of AF are incompletely understood and that the arrhythmogenicity of fibrotic tissue is likely related to the fibrotic substrate's characteristics. Indeed, it is recognised that different forms of fibrosis can co-exist in atrial tissue and that these fibrotic areas may vary in their roles in initiating and maintaining AF, and therefore extensive ablation may not be of benefit (4). The pathophysiology of atrial fibrillation is consequently likely to vary between individuals. This has been recognised by the European Society of Cardiology who have advocated the requirement for a personalised approach to AF management in the future (9). It is also important to add that there is a not a standardised approach to fibrosis-guided ablation and this may lead to variation amongst operators.

Given the results of the initial DECAAF study, it would certainly be interesting to explore whether a fibrosis-guided ablation approach may offer benefit

in selected patient groups. Given the results of the DECAAF II trial, it appears reasonable to conclude that an empirical approach may not confer benefit in first-procedure ablations. However, it would be interesting to explore whether a fibrosis-guided ablation approach may offer benefit in selected repeat procedures or subgroups of the persistent AF population. In the future, atrial MRI could be used 1) to determine the potential likelihood of success of catheter ablation, and 2) to examine whether fibrosis-guided ablation may offer benefit in certain subgroups of AF patients. These hypotheses require further investigation.

One approach to unravel the relationship between cardiac magnetic resonance features of fibrosis and the electrophysiological mechanisms sustaining atrial fibrillation is computational modelling. Computational modelling can utilise anatomical and functional information to understand how electrical conduction occurs within atrial tissue and this can provide an understanding of an individual patient's pathophysiological substrate (10). This offers a promising approach to enable personalised AF ablation procedures in the future. Future advances may allow computational modelling to be utilised to non-invasively identify areas of fibrotic tissue that are important to the maintenance of AF (11). This may enable these areas to be selected for ablation leading to a more targeted fibrosis-guided ablation approach in the future. The Realistic Computational Electrophysiology Simulations for the Targeted Treatment of Atrial Fibrillation (ReCETT-AF) (ClinicalTrials.gov #NCT05057507) study will aim to integrate data from cardiac MRI scans with electroanatomic mapping data to define patient-specific mechanisms of AF. An understanding of patient-specific pathophysiology may enable the design of treatment strategies tailored to the patient. Computational modelling may enable the delivery of a precision-cardiology based approach to AF management and this offers the potential to improve patient outcomes in AF.

Conclusions

The variable efficacy of PVI in the treatment of AF has resulted in the development of numerous novel AF ablation approaches. The DECAAF II study failed to demonstrate benefit when an empirical approach comprising fibrosis-guided ablation was used in conjunction with PVI. The failure of this approach may be representative of the heterogeneity that exists in the initiation and maintenance of AF amongst individual patients. Patient-specific computational modelling may facilitate the delivery of personalised ablation approaches offering the potential to improve outcomes in AF.

Disclosures

No disclosures to declare.

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