ESC European Society of Cardiology

European Heart Journal - Case Reports (2024) **8**, ytae358
https://doi.org/10.1093/ehjcr/ytae358

CASE REPORT
Electrophysiology

Case report of persistent atrial fibrillation with durably isolated pulmonary veins: what's next?

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Received 29 December 2023; revised 22 February 2024; accepted 17 July 2024; online publish-ahead-of-print 23 July 2024

Background Pulmonary vein isolation (PVI) has emerged as a safe and effective treatment for patients with paroxysmal and persistent atrial fibrillation. Nevertheless, in some patients, a relapse of atrial fibrillation occurs although pulmonary veins are durably isolated. For those patients, the underlying mechanisms of atrial fibrillation perpetuation are manifold and optimal treatment options are not yet defined.

Case summary We describe a case of a 55-year-old man with a history of atrial fibrillation and previous PVI presenting with persistent AF and arrhythmia induced cardiomyopathy. During the redo procedure, electro-anatomical mapping revealed durably isolated PV. Bipolar mapping showed large low-voltage areas at the posterior wall and the septum. As the patient was refractory to electrical cardioversion, it was decided to modify the large low-voltage areas as potential arrhythmic substrate. After performing additional ablation with isolation of the posterior wall and two anterior/septal lines, the patient spontaneously converted to sinus rhythm.

Discussion Ablation in patients with persistent AF despite durable PVI remains a challenge for the treating team. Individualized ablation approaches addressing additional arrhythmic substrates or extra-PV triggers can be considered to treat patients with persistent AF and durable PVI.

Keywords Atrial fibrillation • Substrate mapping • Non-pulmonary vein triggers • Case report

ESC curriculum 5.3 Atrial fibrillation • 6.2 Heart failure with reduced ejection fraction

Learning points

- In some patients, atrial fibrillation can persist even with isolated pulmonary veins.
- Unlike the pulmonary vein isolation procedure, the approaches to address the arrhythmic substrate are not standardized and the endpoints less well defined.
- One of the successful strategies to restore sinus rhythm is the modification of low-voltage areas in left atrium.

Introduction

After the groundbreaking findings from Haïssaguerre *et al.*,[1] the isolation of the pulmonary veins (PVI) has become the interventional standard treatment for patients with atrial fibrillation (AF). In patients with persistent AF, the success rates of PVI are lower compared to patients with paroxysmal AF[2] and in some cases, AF persists even after isolation of the pulmonary veins (PV). Many approaches have been evaluated to improve the outcomes in these settings, like posterior wall isolation or additional ablation lines.[3,4] Here, we present a case of a patient with

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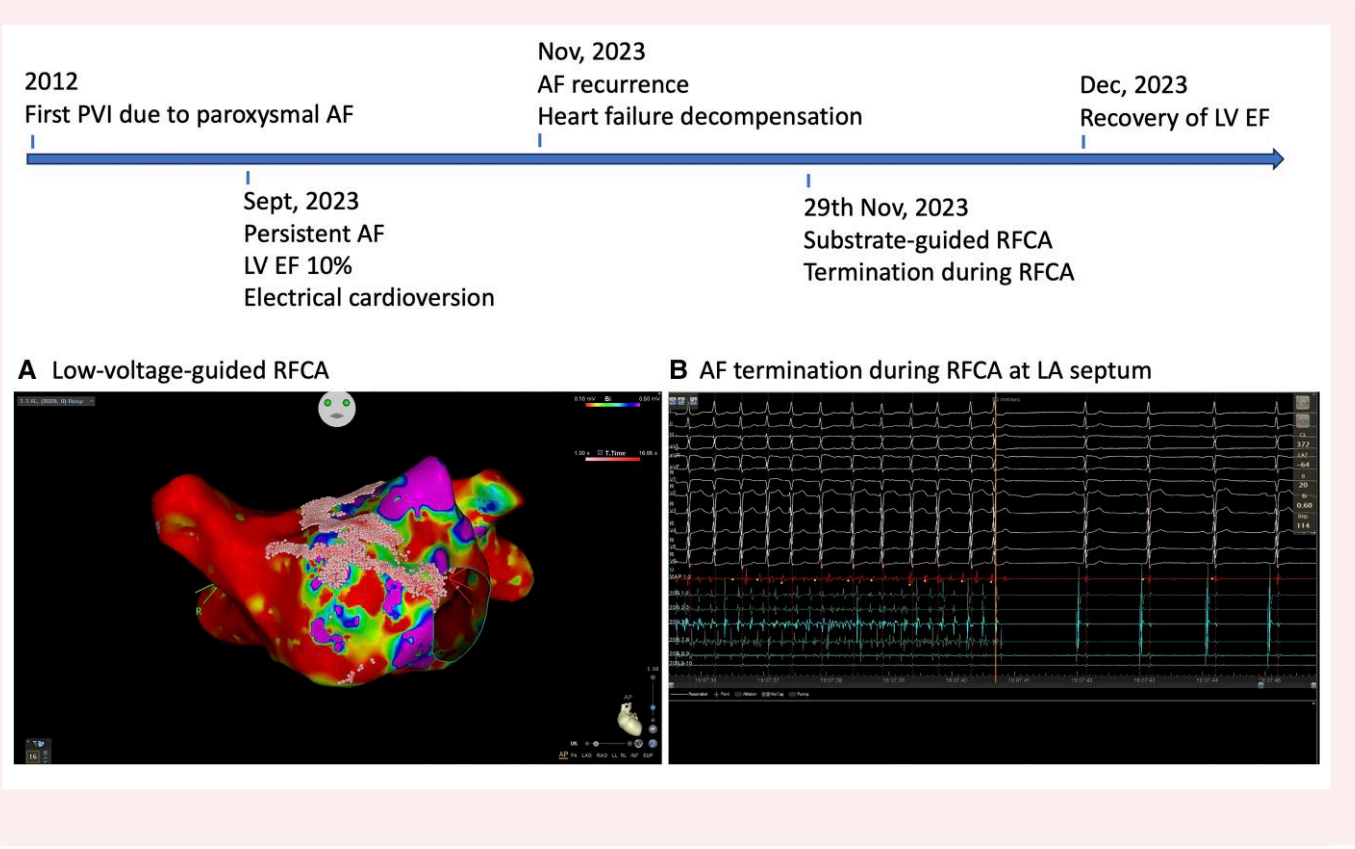
Handling Editor: Andreas Metzner
Peer-reviewers: Sebastian Feickert; Leo Bergau
Compliance Editor: Gal Tsaban

persistent AF despite isolated PVs in whom a successful ablation was achieved by addressing extra-PV substrate.

Summary figure



Case summary

A 55-year-old Caucasian man presented with chest discomfort, dyspnoea, and palpitations. He had a history of paroxysmal AF with a PVI in 2012. Significant comorbidities were an interstitial lung disease, ANCA associated vasculitis, obesity, and obstructive sleep apnoea. Baseline therapy did not include anticoagulation or any antiarrhythmic medication. The electrocardiogram showed AF with tachycardia of 162 b.p.m. Echocardiography revealed globally reduced ejection fraction (EF 10%) and left atrial volume index (LAVI) diameter of 34 mL/m^2. Coronary angiogram showed no significant coronary artery disease. After exclusion of left atrial (LA) thrombi, a successful electrical cardioversion was performed and the patient was scheduled for AF ablation.

When the patient presented for ablation 7 weeks later, he was in AF again. The procedure was performed under deep sedation using midazolam, fentanyl, and propofol. After femoral access, a 10-polar catheter (Biosense Webster, Irvine, USA) was introduced over a short 7 F sheath (Merit Medical 11 cm 7 F Prelude; 6 F) into the coronary sinus. Single transseptal puncture was performed under fluoroscopic guidance and a steerable Agilis-8.5 F transseptal sheath (Abbott, Chicago, USA). The sheath was continuously flushed with heparinized saline (2 mL/h). During the procedure, heparin boluses were administered targeting an activated clotting time of >300 s.

Attempts to restore sinus rhythms by electrical cardioversion remained unsuccessful, and the electro-anatomical mapping (CARTO 3, v7.3, Biosense Webster, Irvine, USA) was performed in AF using a multipolar mapping catheter (Pentaray, Biosense Webster, Irvine, USA). Left atrial high-density mapping revealed durably isolated PVs as well as large low-voltage areas (LVA) (≤0.5 mV) at the posterior wall and septum (*Figure 1A–C*). Because of the durable PV isolation, we decided to perform ablation of the extensive LVA as a potential arrhythmic substrate. We used an irrigated contact force catheter (Thermocool Smarttouch SF®, Biosense Webster, Irvine, USA) with 30 W at the posterior and 40 W at the anterior wall. A modified box lesion was applied as shown in *Figure 2A*. Low-voltage areas at the septum were addressed by lines from the mitral valve annulus to the right superior PV and from the mitral valve annulus to the roof line (*Figure 2B and C*). During ablation at the septum, close to the right PV, atrial fibrillation suddenly converted to sinus rhythm (*Figure 2D*). Afterwards the ablation lines were completed. Lines were checked for completeness by differential site pacing manoeuvres.

The patient was discharged 2 days later in sinus rhythm on oral anticoagulation with apixaban and without specific antiarrhythmic medication. Left ventricular ejection fraction had fully recovered. On three-month follow-up, the patient presented in sinus rhythm with normal ejection fraction in good functional status.

Discussion

In 1998, Haïssaguerre *et al.*[1] reported that the pulmonary veins are an important source of ectopic beats, initiating AF. Since then, multiple studies confirmed the benefit of PVI and it has become the cornerstone of AF ablation.[5,6] Therefore, the main cause for AF recurrence after PVI is considered to be the reconnection of the PVs.[7] However, in some individuals, AF can persist even with isolated PVs and several alternative strategies have been tried to manage them, including ablation of complex fractionated atrial electrograms, linear lesions, rotors, and ablation

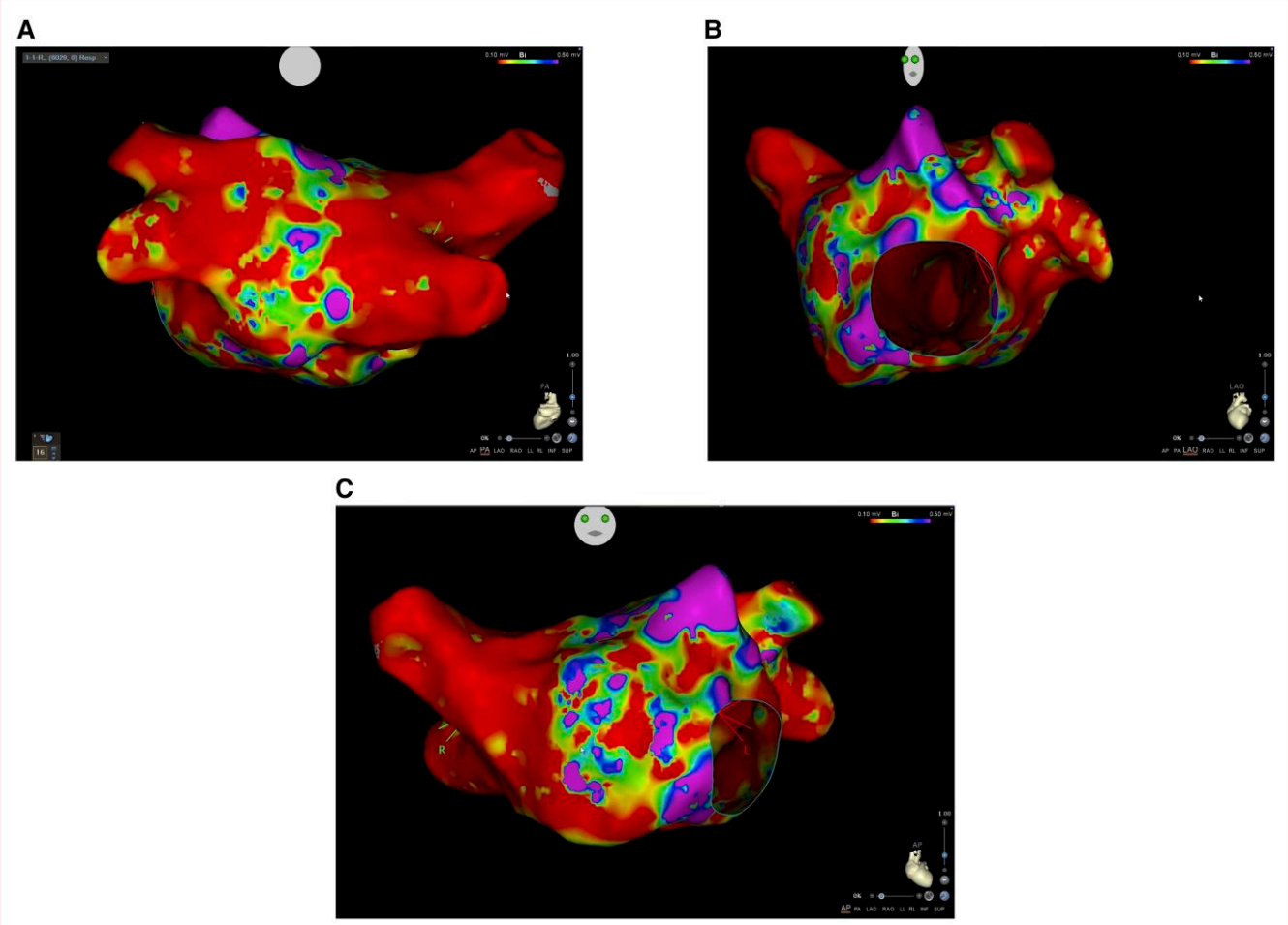


Figure 1 Bipolar voltage map indicates complete pulmonary vein isolation. Large low-voltage areas were seen at the posterior wall and the interatrial septum. Bipolar thresholds were defined as healthy myocardium > 0.5 mV (purple), low-voltage areas ≤ 0.5–0.1 mV (green and yellow), and scar < 0.1 mV (red). (*A*) View from posterior, (*B*) left anterior oblique, and (*C*) anterior.

of extra-PV triggers.[3,4,8] Importantly, none of them has been proved superior to the others. In addition to the catheter ablation, some comorbidities can contribute to the LA remodelling and must be addressed to achieve best outcomes after ablation.

The prospective multicentre observational DECAAF study found the presence of LA fibrosis, estimated by delayed enhancement MRI, to be independently associated with AF recurrence.[9] In experimental models, it was shown that atrial fibrosis leads to increased AF burden as it might serve as an additional PV trigger,[10] and it is essential to perpetuate atrial fibrillation.[11] The DECAAF II trial investigated whether additional ablation of LA fibrosis detected by late gadolinium enhancement (LGE)-MRI was superior to PVI alone. However, it failed to demonstrate benefits regarding arrhythmia recurrence for the fibrosis ablation group. This outcome questioned the effectiveness of CMR-guided approach to AF substrate modification.[12] Comparable results come from the STAR AF II trial where complex fractionated electrograms were ablated as a surrogate for an arrhythmic substrate.[13] Unlike the endpoint of a PVI procedure (electrical isolation of all PVs), the approaches to address an arrhythmic substrate are not standardized and an endpoint of the procedure is not defined, which might contribute to these disappointing results.

On the other hand, a widely accepted way to assess LA fibrosis is electro-anatomical bipolar voltage mapping that can reveal areas of low-voltage fragmented potentials and lines of block. In contrast to the DECAAF-2 and STAR AF II, the recently published randomized multicentre ERASE-AF trial showed improved outcomes after individualized ablation of low-voltage myocardium in addition to PVI compared to PVI alone.[14] The effectiveness of low-voltage based LA substrate modification to address the recurrences in persistent AF in ERASE-AF was clearly demonstrated in our case.

In our patient, we had a case of decompensated heart failure due to AF induced cardiomyopathy so that AF ablation was clearly indicated.[3] During the ablation procedure, two major challenges occurred. On the one hand, persistent durable PVI was present and on the other hand, the patient was refractory to electrical cardioversion. Considering the extensive low-voltage areas posteriorly and at the septum, we decided to modify it by creating lines through the LA low-voltage areas while hoping for organization of the AF in a mappable atrial flutter. To our surprise, the AF terminated suddenly without any transformation to LA macro-re-entry tachycardia that suggested a localized extra-PV trigger.

As mentioned above, AF is caused by an interaction of an initiating trigger and an underlying substrate perpetuating the ongoing arrhythmia. In our case, the low-voltage areas indicated extensive LA remodelling caused by the combination of comorbidities like vasculitis, obesity, and obstructive sleep apnoea. The spontaneous termination of AF during the completion of the septal line suggests several potentials physiological mechanisms of AF in this patient: (1) presence of localized extra-PV

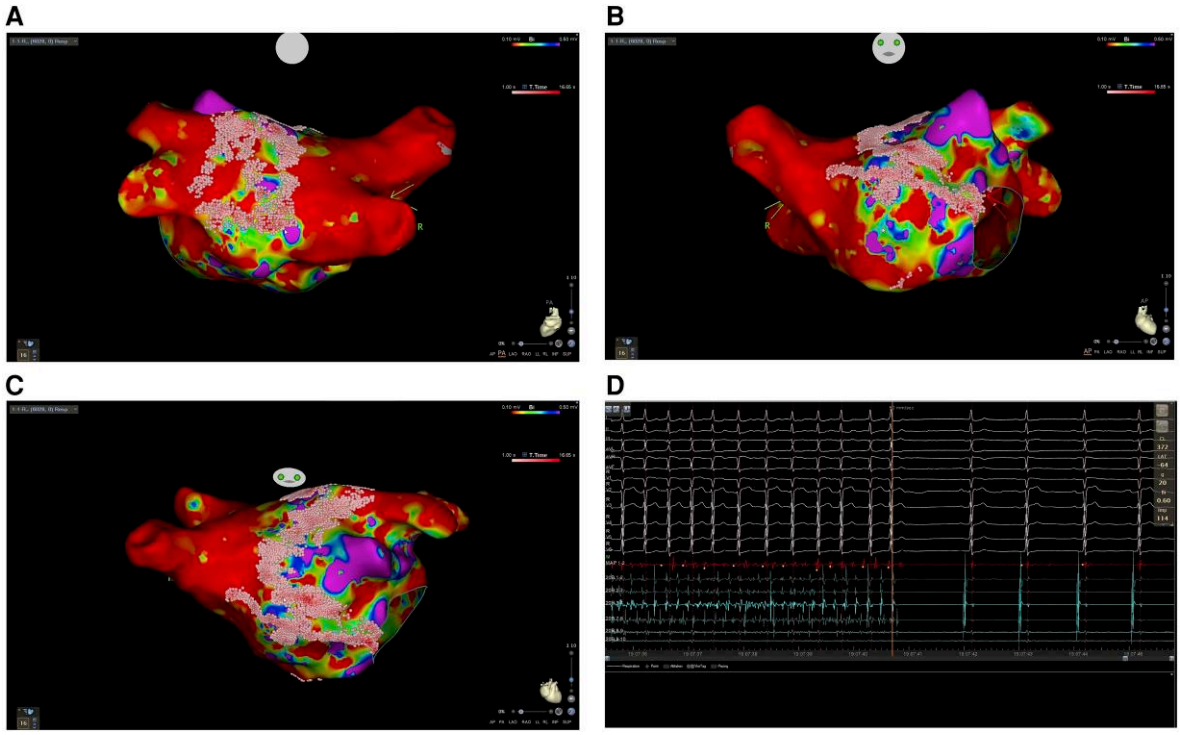


Figure 2 Extensive substrate modification with (*A*) box lesion and posterior wall isolation (posterior–anterior view), (*B*) two anterior lines at the interatrial septum (anterior–posterior view), and (*C*) roof line (view from cranial). (*D*) Modification of arrhythmic substrate led to spontaneous AF termination.

trigger at the septum or (2) extensive LA electrical or fibrotic remodelling predisposing for multiple wavelets at septum, and (3) participation of local ganglionated plexus or (4) presence of epicardial connections. In certain patients with persistent AF, extensive and tailored substrate-based ablation by can be effective to eliminate both trigger and substrate to an extend leading to restoration of sinus rhythm.

Conclusion

Ablation in patients with persistent AF despite durable PVI remains a challenge for the treating team. Individualized ablation approaches addressing additional arrhythmic substrates or extra-PV triggers can be considered to treat patients with persistent AF and durable PVI. Nevertheless, there is still a lot of research to do to finally have clear recommendations how to treat these patients.

Lead author biography

Dr Philipp Bengel is a cardiologist and electrophysiologist. He completed his training in electrophysiology at the University of Göttingen. At present, he is a senior consultant at the Electrophysiology Section of University Hospital of Giessen, Germany. Dr Bengel is a member of the EHRA and DGK. His research interest is the field of late sodium channel NaV1.8 and its role for arrhythmogenesis in heart failure.

Acknowledgements

We thank our colleagues and nurses in the electrophysiology department for their support.

Consent: The authors confirm that written consent for submission and publication of this case including images and associated text has been obtained from the patient in compliance with COPE guidelines.

Conflict of interest: None declared.

Funding: None declared.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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