

Old stuff still trending: use of propafenone as a safety net until catheter ablation in a patient with documented pre-excited atrial fibrillation and Wolff–Parkinson–White syndrome – a classic case report

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Background

Atrial fibrillation in Wolff–Parkinson–White syndrome may result in life-threateningly rapid antegrade conduction over a bypass tract, manifested by an irregular broad-complex (pre-excited) tachycardia that can degenerate to ventricular fibrillation. The shortest pre-excited RR interval below 250 ms during atrial fibrillation (AF) predicts increased risk of sudden cardiac death.

Case summary

We report a case of a 43-year-old man with unremarkable cardiac history who presented due to sudden-onset feeling of palpitations and pre-syncope after strenuous lifting. Electrocardiography depicted fast pre-excited AF. The shortest pre-excited RR interval was estimated at 160 ms, indicating an accessory pathway (AP) with short antegrade refractory period at risk for mediating sudden cardiac death. Direct current cardioversion restored sinus rhythm unravelling delta waves. The patient was put on propafenone 450 mg/day having an uneventful clinical course. On Day 10 post-admission, electrophysiological study induced rapid AF but the shortest pre-excited RR interval was substantially increased to 264 ms. A left anterolateral AP was ablated. The patient remained symptom free until his latest follow-up in the 3rd-month post-ablation without manifest pre-excitation on the surface electrocardiogram.

Discussion

Treatment options of pre-excited AF include anti-arrhythmic agents but mainly electrical cardioversion. Cardioversion can safely restore sinus rhythm, while use of anti-arrhythmics often requires intensive care unit monitoring due to the risk of QT prolongation. Catheter ablation is the mainstay of therapy for symptomatic patients. Our rare report highlights the direct impact of propafenone on prolonging the refractoriness of the AP, effectively and safely, and reappraises propafenone’s worthiness as a protective measure following pre-excited AF episode until ablation.

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Keywords

Wolff–Parkinson–White syndrome • Pre-excited atrial fibrillation • Shortest pre-excited RR interval—SPERRI • Propafenone • Classic case report

ESC Curriculum

5.1 Palpitations • 5.3 Atrial fibrillation • 7.1 Haemodynamic instability • 5.5 Supraventricular tachycardia

Learning points

- Propafenone could be offered to patients with Wolff–Parkinson–White syndrome after a documented episode of pre-excited atrial fibrillation (AF) with exceptionally short pre-excited RR interval as a bridge to ablation and safety net to avoid risk of ventricular fibrillation and sudden death.
- Irregularly irregular wide-QRS complex tachycardia should set the diagnosis of pre-excited AF and emergency physicians should be capable of recognizing this unique electrocardiogram demonstration immediately.
- Direct current cardioversion remains the gold standard therapy for fast broad irregular tachycardia in the acute phase followed by a pathway ablation in an experienced centre.

Introduction

Wolff–Parkinson–White (WPW) syndrome is a congenital condition referring to the Kent bundle; an accessory pathway (AP) providing direct cohesion between atrial and ventricular myocardium constructing a route for re-entrant tachycardia circuits.¹ It encompasses the combination of overt electrocardiographic pre-excitation (short PR, QRS with the *delta* wave, repolarization abnormalities) in the presence of sinus rhythm.¹ Wolff–Parkinson–White's unique characteristic is AP's ability to conduct in a bidirectional fashion; either retrogradely resulting in atrioventricular re-entry tachycardias (AVRT) of narrow QRS complexes or antegradely, originating wide QRS tachydysrhythmias like antidromic AVRT or pre-excited atrial fibrillation (AF) and atrial flutter. Malignant degeneration to ventricular fibrillation (VF) can emerge.² Accessory pathway electrical properties and effects on atrial architecture along with increased atrial vulnerability and atrial myopathy constitute the underlying mechanisms in the pathogenesis of AF in these patients; spontaneous degeneration of AVRT may potentially trigger AF as well.³ Advanced age with two peaks at the 3rd and 5th decade of life, male sex, and prior history of syncope independently predispose WPW patients to AF.⁴

Many studies distinguished the benefit of propafenone's administration (or class Ic agents in general) in patients with WPW syndrome.^{5–8} Although propafenone exerts unique prolonging effect on AP conduction and remarkable 'anti-atriofibrillatory' activity,^{5–7} clinicians are usually reluctant to prescription due to proarrhythmic effects and non-negligible risk of converting AF to 1:1 atrial flutter.⁹ In this report, we aim to communicate propafenone's short-term favourable electrophysiological properties on AP refractoriness and reconsider its value in non-tertiary centres as a safety net for WPW patients documenting fast pre-excited AF, until electrophysiological study is performed.

Timeline

Day 1 Hospital admission	Near syncope, pre-excited AF with rapid ventricular response and shortest pre-excited RR interval (SPERRI) at 160 ms, immediate transfer to the cardiac intensive care unit (ICU).
Cardiac ICU	Light sedation with 5 mg midazolam. Direct current cardioversion with 270 Joules restored sinus rhythm with manifest pre-excitation. Wolff–Parkinson–White syndrome diagnosed. Uneventful recovery within several minutes. Anticoagulation with enoxaparin 80 mg b.i.d. (from Day 1 to Day 9).
Day 2 Cardiology ward	Complete blood count, cardiac troponin, d-dimers, thyroid-stimulating hormone: values within normal range. Transthoracic echocardiography: normal left and right ventricular function and dimensions, no valvular lesions or septal defects. X-ray imaging of the lungs: clear. Start on propafenone 150 mg t.i.d. (from Day 2 to Day 9).
Day 3	No QRS widening.
Day 8	Transfer to a tertiary EP centre.
Day 10	Electrophysiological study with local anaesthesia (20 mg of lidocaine

Continued

	subcutaneously) for sheath insertion; no sedation was required. SPERRI 264 ms. Catheter ablation of a left anterolateral accessory pathway. Sodium heparin (5000 U bolus and 1000 U/h) for anticoagulation during electrophysiological study.
Day 11	Discharged on rivaroxaban 20 mg for a month.
One month of follow-up	Symptom free, no pre-excitation on surface electrocardiogram, rivaroxaban stopped, family members screened for pre-excitation.
Three months of follow-up	Symptom free. Recommendation for periodic follow-up.

measured 90/70 mmHg, oxygen level 99%, heart-rate 210–230 b.p.m., and body temperature 36.6°C. Past medical history was clear for cardiac disease, syncope, or pre-syncope. No history of sudden cardiac death (SCD) or cardiomyopathy into his family was stated. He denied recent flu-like symptoms, smoking, illicit drug use, or excessive alcohol consumption. Physical examination was unremarkable. Initial electrocardiogram (ECG) depicted an irregularly irregular, broad QRS complex tachycardia (Figure 1). No previous ECG recordings were handed. Direct current (DC) cardioversion restored sinus rhythm with manifest ventricular pre-excitation and clear 'delta' waves (Figure 2) confirming our initial clinical suspicion for underlying WPW syndrome. Shortest pre-excited RR interval (SPERRI) during AF was estimated at 160 ms (Figure 1), indicating an AP with extremely short antegrade effective refractory period (ERP) at risk for mediating SCD. Echocardiography ruled out abnormalities associated with WPW, including Ebstein's anomaly, valve lesions, cardiac hypertrophy, atrial aneurysms, and septal defects.² Cardiac ischaemia was also excluded on the basis of clinical, electrocardiographic, echocardiographic, and laboratory data. The patient was put on enoxaparin 80 mg b.i.d. and propafenone 150 mg t.i.d. and his clinical course remained uneventful. Electrophysiological study (EPS) was performed at a tertiary centre on Day 10 post-diagnosis; programmed atrial stimulation induced pre-excited AF with markedly increased SPERRI = 264 ms and a left

Case presentation

A 43-year-old man presented to the emergency department reporting sudden-onset feeling of palpitations and near syncope after strenuous heavy lifting. He was pale and diaphoretic; blood pressure was

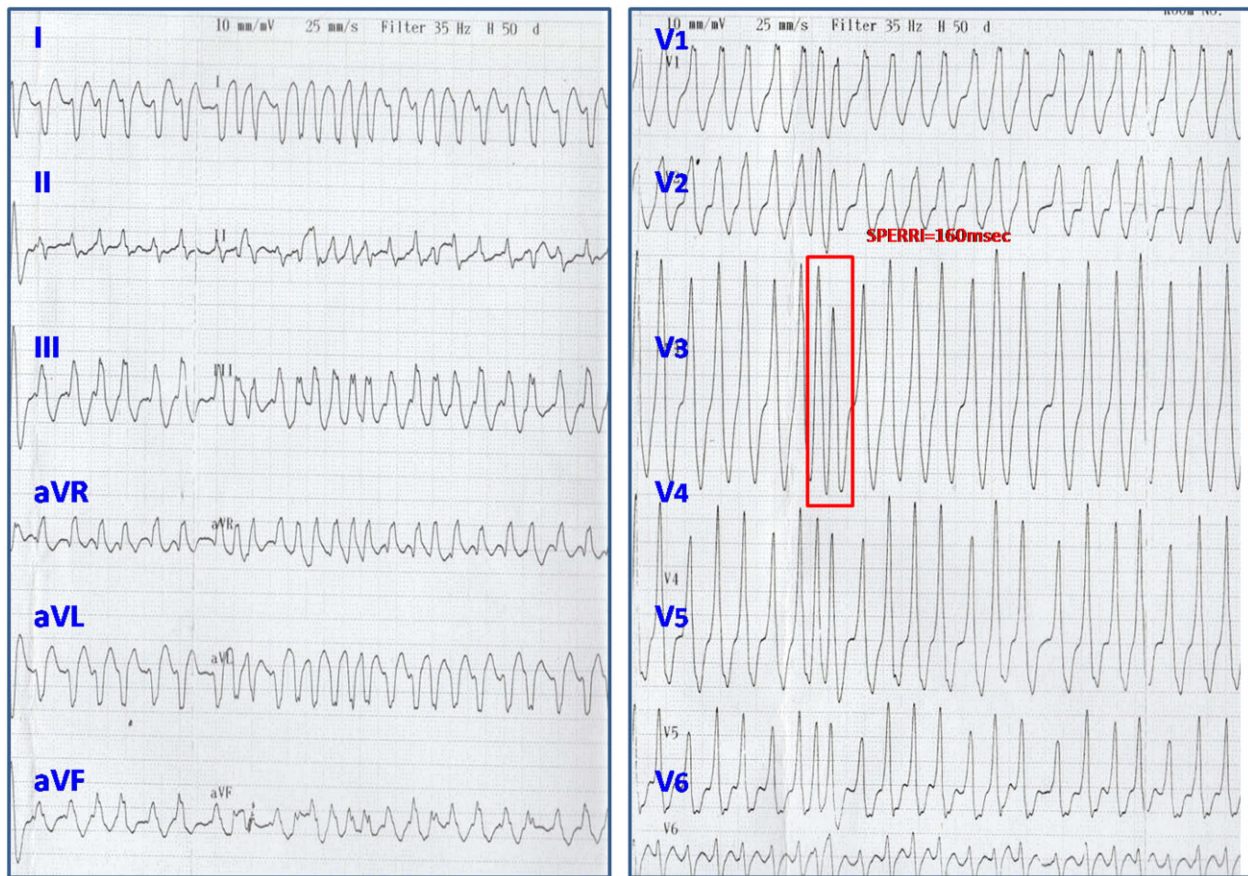


Figure 1 Electrocardiogram upon presentation demonstrating an irregular, wide QRS complex tachycardia consistent with Wolff–Parkinson–White syndrome with pre-excited atrial fibrillation, with the shortest pre-excited RR interval (SPERRI) measured at 160 ms.

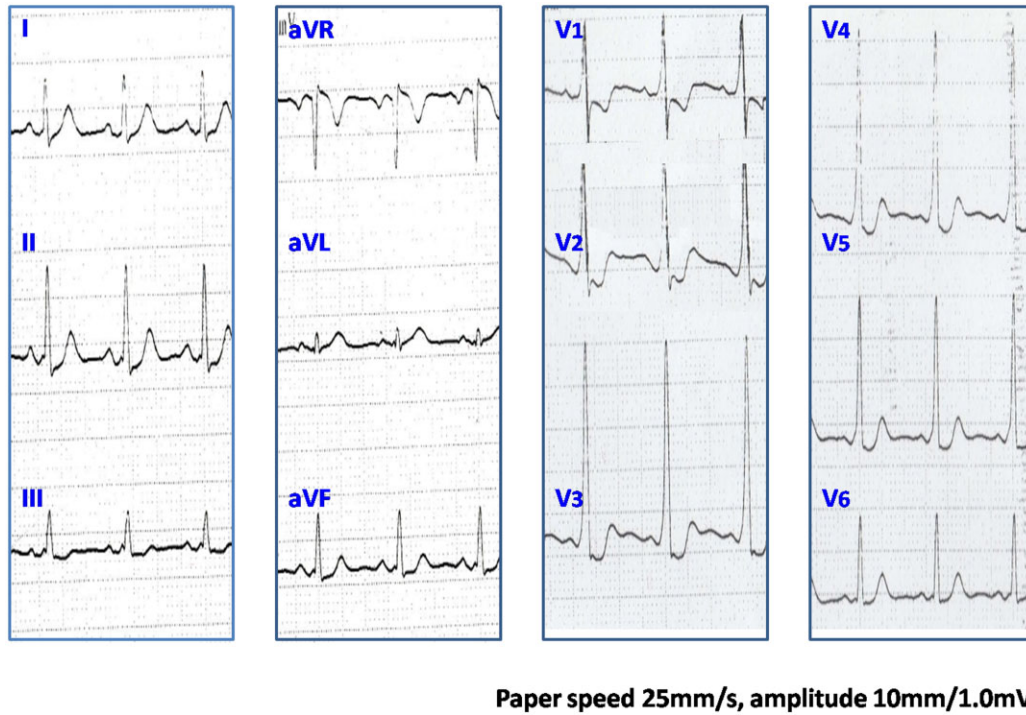


Figure 2 Electrocardiogram immediately after direct current cardioversion illustrating classic Wolff–Parkinson–White findings: short PR interval (<120 ms), wide QRS complex (>120 ms) with slurred onset of the QRS waveform (*delta* wave); and secondary ST-T wave changes of abnormal repolarization directed opposite the major *delta* wave and QRS complex. By using the stepwise approach proposed by the St George’s algorithm [absence of negative QRS in both III and V1 leads (Step 1); positive QRS complex in aVL (Step 2); and positive QRS complex in V1 (Step 3)], a left anterolateral AP was tracked.²

anterolateral AP with antegrade only conduction properties was ablated (Figures 3–5). The patient was scheduled for routine cardiologic follow-up and advised to abstain from intense physical activity for at least 1-month post-discharge.² In case of palpitations, ECG and 24-h Holter monitoring were suggested. CHA₂DS₂-VASc Score was calculated zero, so 1 month of rivaroxaban 20 mg daily was deemed sufficient post-ablation.¹⁰ Family members were also screened for pre-excitation. The patient remained symptom free without pre-excitation on surface ECG on his latest follow-up visit 3 months after the procedure.

Discussion

In this report of WPW syndrome manifested by life-threatening pre-excited AF, we wish to highlight old-school medicine knowledge of using propafenone as a short-term protective measure in preventing relapses of pre-excited arrhythmias/AF and/or SCD until ablation. In our specific patient, propafenone prolonged SPERRI from 160 ms on presentation, indicating increased risk for SCD, to 264 ms during EPS, surpassing borderline safety limit (250 ms) within only 10 days.² This remark seems important underlining rapid and drastic modification of AP refractoriness. No AF relapses or atrial flutter episodes⁹ were recorded, emphasizing propafenone’s short-term ‘anti-atriofibrillatory’ effects without adverse impact on atrioventricular nodal (AVN)

conduction. In this respect, administration of propafenone could be encouraged, especially in non-tertiary care facilities, as a safety net until EPS. Pre-defined connecting pathways for patient transfer to experienced EP centres should be established.

In our case, ECG upon presentation (Figure 1) depicted a grossly irregular, wide QRS complex tachycardia with atypical RBBB morphology.² Differential diagnosis of this bizarre-looking tachycardia should include AF with antegrade conduction over an AP, polymorphic ventricular tachycardia (VT) or atrial tachycardia with variable degree block and aberrancy. Pre-excited AF demonstrates irregularity, a greater beat-to-beat variability and erratic QRS morphology due to alternate degrees of fusion and activation over both the AP and the AVN; however, unlike polymorphic VT or torsades de pointes, it maintains a stable axis without twisting. If still in doubt about clarification, electrocardioversion should be opted.²

Paroxysmal AF accounts for ~50% of WPW patients with fateful events.¹¹ These patients are typically young without structural heart disease and usually present with haemodynamic instability, requiring urgent cardioversion, and early AP ablation.¹² The AP is of primary importance in the induction of spontaneous AF and decreased incidence of AF recurrence is reported after successful AP elimination.³ In this respect, AP over pulmonary veins ablation was prioritized in our relatively young patient with low 10-year Atherosclerotic Cardiovascular Disease Risk (ASCVD) Score (1.2%) and zero CHA₂DS₂-VASc Score.^{2,3} The risk of SCD in WPW syndrome is

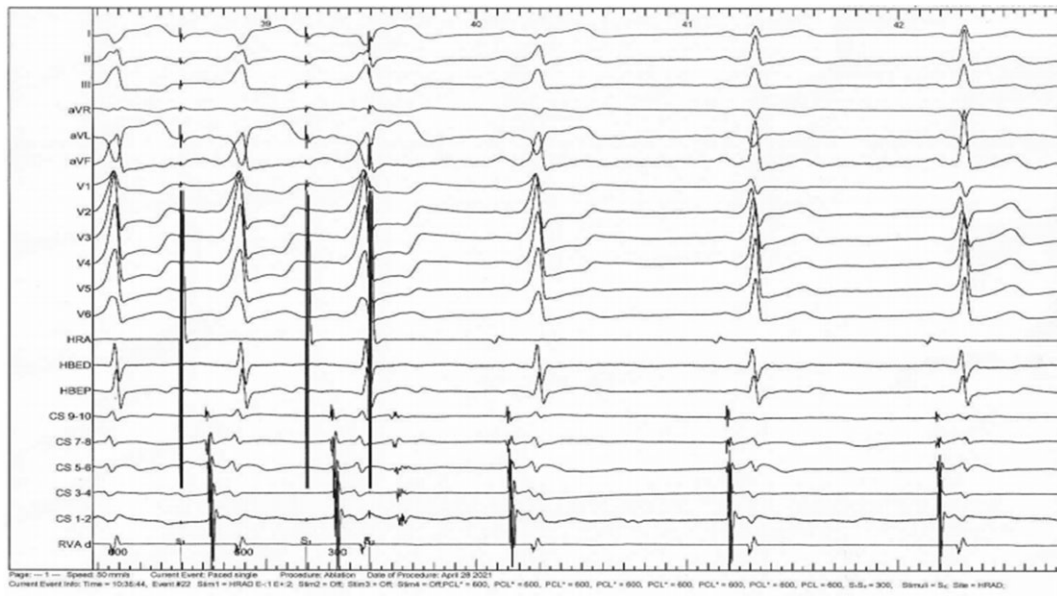


Figure 3 Atrial stimulation (S1 = 600 ms) during the electrophysiological study performed on Day 10 post-diagnosis, illustrating that (i) the antegrade earliest ventricular activation site was at CS1-2 dipole, indicating a left anterolateral location of the accessory pathway and (ii) the antegrade accessory pathway effective refractory period was 300 ms.



Figure 4 Pre-excited atrial fibrillation induced during the electrophysiological study [rapid atrial pacing with drive train (S1) at 600 ms followed by an extrastimulus (S2) at a coupling interval of 280 ms]. The shortest pre-excited RR interval (SPERRI) was calculated at 264 ms.

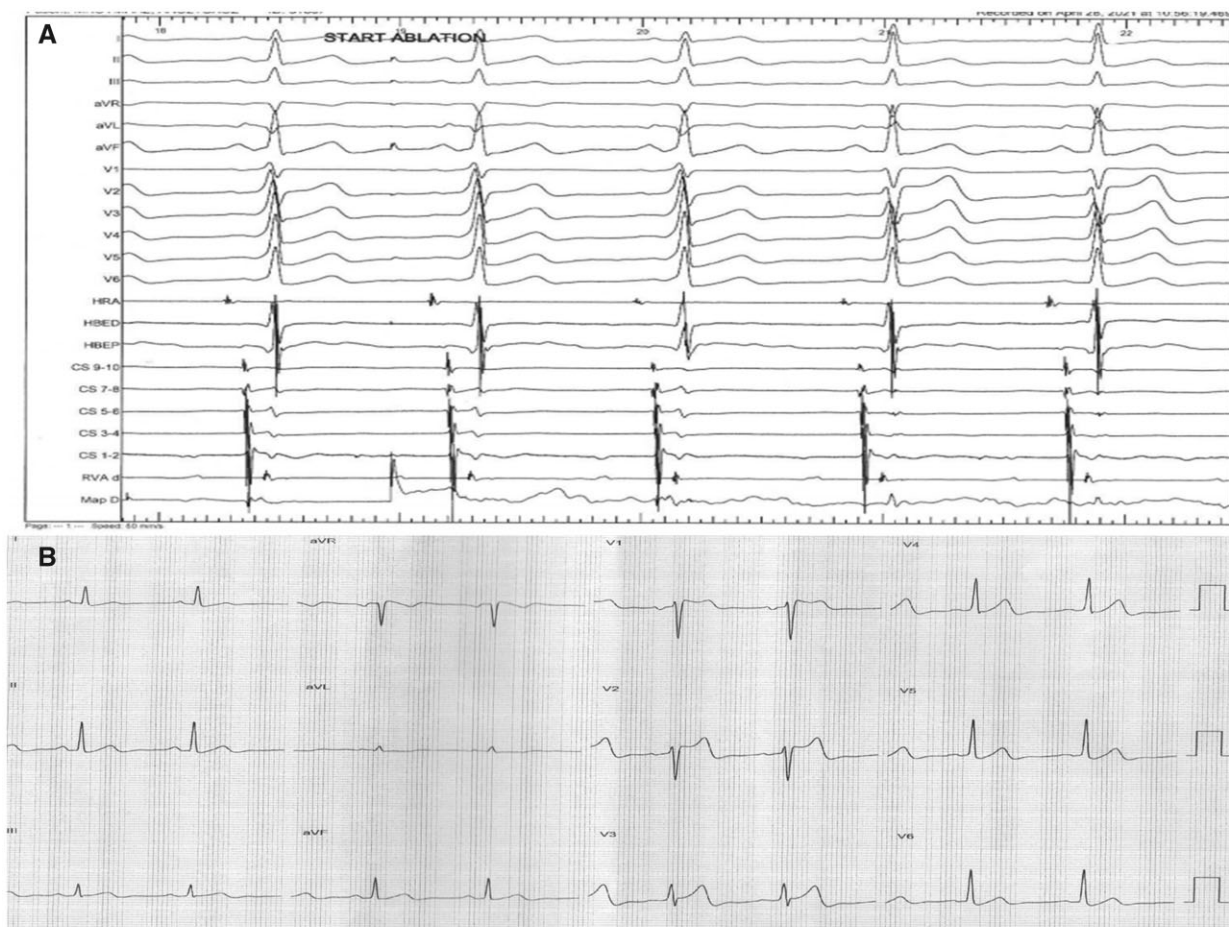


Figure 5 (A) Intracardiac electrograms during accessory pathway ablation with 40 W radio-frequency lesion targeted at the earliest activation (fused atrial and ventricular signals) at the lateral mitral annulus (transeptal approach); rapid loss of pre-excitation (please observe the 4th and 5th QRS complexes) immediately after initiation of ablation is clearly depicted. (B) Post-ablation surface electrocardiogram also illustrating loss of pre-excitation (absence of 'delta' waves).

increased if multiple APs are present, short AP ERP (<240 ms) is measured, AF and atrial flutter are established, or a family history of premature SCD is mentioned. However, SCD occurs as the first and only symptom in only <1% of WPW patients.^{11–13}

On admission, DC cardioversion (preferred over ibutilide or procainamide necessitating complex haemodynamic/intensive care unit monitoring) resumed sinus rhythm, unveiling an overt (manifest) left anterolateral AP according to St George's algorithm.² Accessory pathways may be located in the left (most commonly) or right free wall or septum; in 5–10% of patients, multiple pathways are present.² In our specific patient, left-sided AP position and intact tricuspid valve (TV) apparatus on echocardiography ruled out Ebstein's anomaly as this entity is commonly associated with right-sided APs and TV abnormalities. In up to 50% of WPW cases, APs are electrocardiographically silent (concealed), as they conduct only retrogradely perpetuating an orthodromic AVRT²; in this setting, propafenone can increase antegrade ERP, widening the tachycardia zone thus making macro-re-entry more likely. Instead, APs propagating impulses only

in the antegrade direction, like in our case, are quite uncommon ($\leq 10\%$)²; in this specific subset, we can *ex juvantibus* postulate that propafenone is safe and propitious, especially when ablation is not feasible.

Propafenone has been reported to minimize AF induction or prevent pre-excited AF by SPERRI elongation, resume sinus rhythm or decrease markedly peak ventricular rate during AF and terminate or slow ventricular response of inducible AVRT.^{5–7} Its unique 'anti-atriofibrillatory' effect along with its prolonging action on AP refractoriness slowing or blocking conduction in both antegrade and retrograde direction,^{5–7} qualified administration. Possibly, Ic agents in general could have also functioned well in our patient as they share similar electrophysiological effects on normal conduction system and APs.¹⁴ Although our data may suggest a significant short-term impact of propafenone on SPERRI prolongation, sympathetic over-discharge upon presentation may have underestimated initial SPERRI measurements. In addition, sedative protocols and parasympathetic stimulation may influence EPS SPERRI calculations and overrate propafenone's effect;

however, in our case, no sedative agents were administered. During the acute phase, nodal blocking agents were sidestepped because of imminent degeneration to VF, facilitating conduction via the AP.¹² Following stabilization, propafenone's additional b-blocker effect (compared with other Ic agents) may have prevented adverse arrhythmic events, including 1:1 atrial flutter.^{14,15} Although not confirmed in our specific patient, oral use has been associated with long-term benefits, by preventing symptomatic arrhythmias or modifying recurrent ones, making them rarer, slower, or prone to self-termination.^{5,6} Validated data render propafenone fairly safe overall; significant electrophysiological side effects and proarrhythmia with enduring use have been reported in 1.9%, while SCD in 0.6% with underlying WPW syndrome or structural heart disease.¹⁶

Conclusion

Specific ECG morphology should set the diagnosis of pre-excited AF. Direct current cardioversion is preferred over anti-arrhythmic drugs. Propafenone could come back in trend out of our armamentarium and be used at least for short term as a bridge to the EP lab. Its remarkable effects prolonging AP ERP and SPERRI, depressing atrial arrhythmias, along with sympathoplegic and b-blocking action, establish it as an old but gold agent in interim prevention of AF recurrences and SCD. Ablation, though, remains the ultimate therapy.

Lead author biography



Dr Dimitrios Karelis is a junior cardiology trainee at the Cardiology Department of Trikala Hospital in Greece. He obtained his medical degree from the University of Patras in 2019 and he is currently undertaking his MSc in 'Thrombosis and Antithrombotic Treatment'. Research Interests: Arrhythmias, Platelets and Thrombosis, Cardio-oncology, Heart failure, and Transplantation.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

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

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References

- Wolff L, Parkinson J, White PD. Bundle-branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. *Am Heart J* 1930;**5**: 685–704.
- Brugada J, Katritsis DG, Arbelo E, Arribas F, Bax JJ, Blomström-Lundqvist C et al.; ESC Scientific Document Group. 2019 ESC Guidelines for the management of patients with supraventricular tachycardia: the Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC). *Eur Heart J* 2020;**41**:655–720.
- Centurión OA, Shimizu A, Isomoto S, Konoe A. Mechanisms for the genesis of paroxysmal atrial fibrillation in the Wolff Parkinson-White syndrome: intrinsic atrial muscle vulnerability vs. electrophysiological properties of the accessory pathway. *Europace* 2008;**10**:294–302. PMC[10.1093/europace/eun031] [18308751]
- Szumowski Ł, Walczak F, Urbank P, Szufladowicz E, Ratajska E, Kepski R et al. Risk factors of atrial fibrillation in patients with Wolff-Parkinson-White syndrome. *Kardiol Pol* 2004;**60**:206–216; discussion 217.
- Ludmer PL, McGowan NE, Antman EM, Friedman PL. Efficacy of propafenone in Wolff-Parkinson-White syndrome: electrophysiologic findings and long-term follow-up. *J Am Coll Cardiol* 1987;**9**:1357–1363.
- Breithardt G, Borggrete M, Wiebringhaus E, Seipel L. Effect of propafenone in the Wolff-Parkinson-White syndrome: electrophysiologic findings and long-term follow-up. *Am J Cardiol* 1984;**54**:29D–39D.
- Boahene KA, Klein GJ, Yee R, Sharma AD, Fujimura O. Termination of acute atrial fibrillation in the Wolff-Parkinson-White syndrome by procainamide and propafenone: importance of atrial fibrillatory cycle length. *J Am Coll Cardiol* 1990;**16**:1408–1414.
- Núnain SO, Camm AJ, Ward DE. Treating Wolff-Parkinson-White syndrome. *BMJ* 1991;**303**:1411–1412.
- el-Harari MB, Adams PC. Atrial flutter with 1:1 atrioventricular conduction caused by propafenone. *Pacing Clin Electrophysiol* 1998;**21**:1999–2001.
- Blanc JJ, Almendral J, Brignole M, Fatemi M, Gjesdal K, González-Torrecilla E et al.; Scientific Initiatives Committee of the European Heart Rhythm Association. Consensus document on antithrombotic therapy in the setting of electrophysiological procedures. *Europace* 2008;**10**:513–527.
- Etheridge SP, Escudero CA, Blaufox AD, Law IH, Dechert-Crooks BE, Stephenson EA et al. Life-threatening event risk in children with Wolff-Parkinson-White syndrome: a multicenter international study. *JACC Clin Electrophysiol* 2018;**4**:433–444.
- Fujimura O, Kuo CS, Smith BA. Pre-excited RR intervals during atrial fibrillation in the Wolff-Parkinson-White syndrome: influence of the atrioventricular node refractory period. *J Am Coll Cardiol* 1991;**18**:1722–1726.
- Brembilla-Perrot B, Pauriah M, Sellal JM, Zinzus PY, Schwartz J, de Chillou C et al. Incidence and prognostic significance of spontaneous and inducible antidromic tachycardia. *Europace* 2013;**15**:871–876.
- O'Nunain S, Garratt CJ, Linker NJ, Gill J, Ward DE, Camm AJ. A comparison of intravenous propafenone and flecainide in the treatment of tachycardias associated with the Wolff-Parkinson-White syndrome. *Pacing Clin Electrophysiol* 1991;**14**:2028–2034.
- Faber TS, Camm AJ. The differentiation of propafenone from other class Ic agents, focusing on the effect on ventricular response rate attributable to its beta-blocking action. *Eur J Clin Pharmacol* 1996;**51**:199–208.
- JanousEk J, Paul T. Safety of oral propafenone in the treatment of arrhythmias in infants and children (European retrospective multicenter study). Working Group on Pediatric Arrhythmias and Electrophysiology of the Association of European Pediatric Cardiologists. *Am J Cardiol* 1998;**81**:1121–1124.