Direct thrombin inhibition during pulmonary vein isolation using pulsed field ablation

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Introduction

Bivalirudin reversibly inhibits circulating and clot-bound thrombin, while also inhibiting thrombin-mediated platelet activation and aggregation with a predictable antithrombotic response.[1] Some reports have described its use during catheter-based arrhythmia ablation procedures using thermal energy, including pulmonary vein isolation (PVI) for atrial fibrillation (AF) treatment.[2–5]

More recently, pulsed field ablation (PFA) has emerged as a promising AF ablation modality with reported stroke rates as low as 0.12% in the largest postapproval study MANIFEST-17K.[6] We present a case of a patient with heparin allergy undergoing a PFA-based PVI procedure using intraprocedural bivalirudin.

Case report

A 72-year-old woman with hypertension and obstructive sleep apnea was referred to our hospital to evaluate treatment options after a diagnosis of symptomatic and drug-refractory paroxysmal AF. She had documented heparin allergy (cutaneous rash), suboptimal response to class Ic antiarrhythmic drugs, beta-blocker-induced symptomatic sinus bradycardia, and corneal deposits after previous prolonged amiodarone use. Her CHA_2DS_2-VA score[7] was 2, and she was receiving anticoagulation therapy with edoxaban 60 mg. A transthoracic echocardiogram showed normal biventricular systolic function with moderate left atrial (LA) enlargement and no valvular abnormalities. Serum creatinine was 0.98 mg/dL. The case was accepted for catheter ablation (PVI) using PFA and intraprocedural bivalirudin. Preprocedural computed tomography was performed to evaluate pulmonary vein (PV) and LA anatomy and to assess for thrombus (Figure 1).

KEYWORDS Pulsed field ablation; Pulmonary vein isolation; Atrial fibrillation; Bivalirudin; Heparin; Thrombin inhibition
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KEY TEACHING POINTS

- Owing to its immediate onset of action and short half-life, bivalirudin is a well-established and evidence-based alternative to heparin during catheter-based procedures.
- The combination of pulsed field ablation–based pulmonary vein isolation procedures in atrial fibrillation and the use of bivalirudin may provide a predictable safety profile, constituting a favorable alternative to heparin.
- Further studies evaluating bivalirudin administration during ablation procedures using different pulsed field ablation systems and manufacturers would be desirable.

The ablation procedure was performed under general anesthesia, with uninterrupted oral anticoagulation therapy. After transseptal puncture, bivalirudin was administered as a 0.75 mg/kg intravenous bolus, followed by a 1.75 mg/kg/h infusion. After 5 minutes, the activated clotting time (ACT)

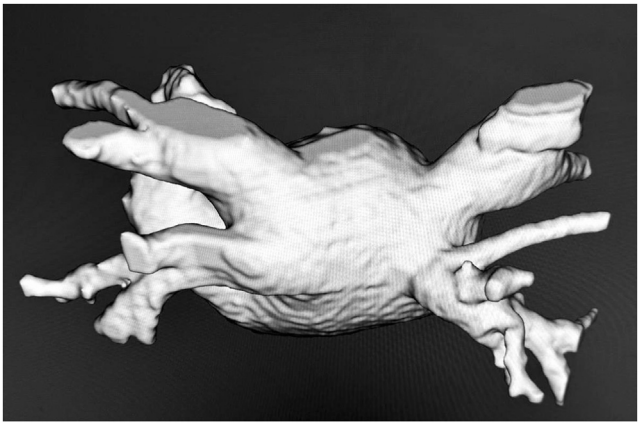

Figure 1 Preprocedural CT reconstruction showing LA and PV anatomy. CT = computed tomography; LA = left atrial; PV = pulmonary vein.

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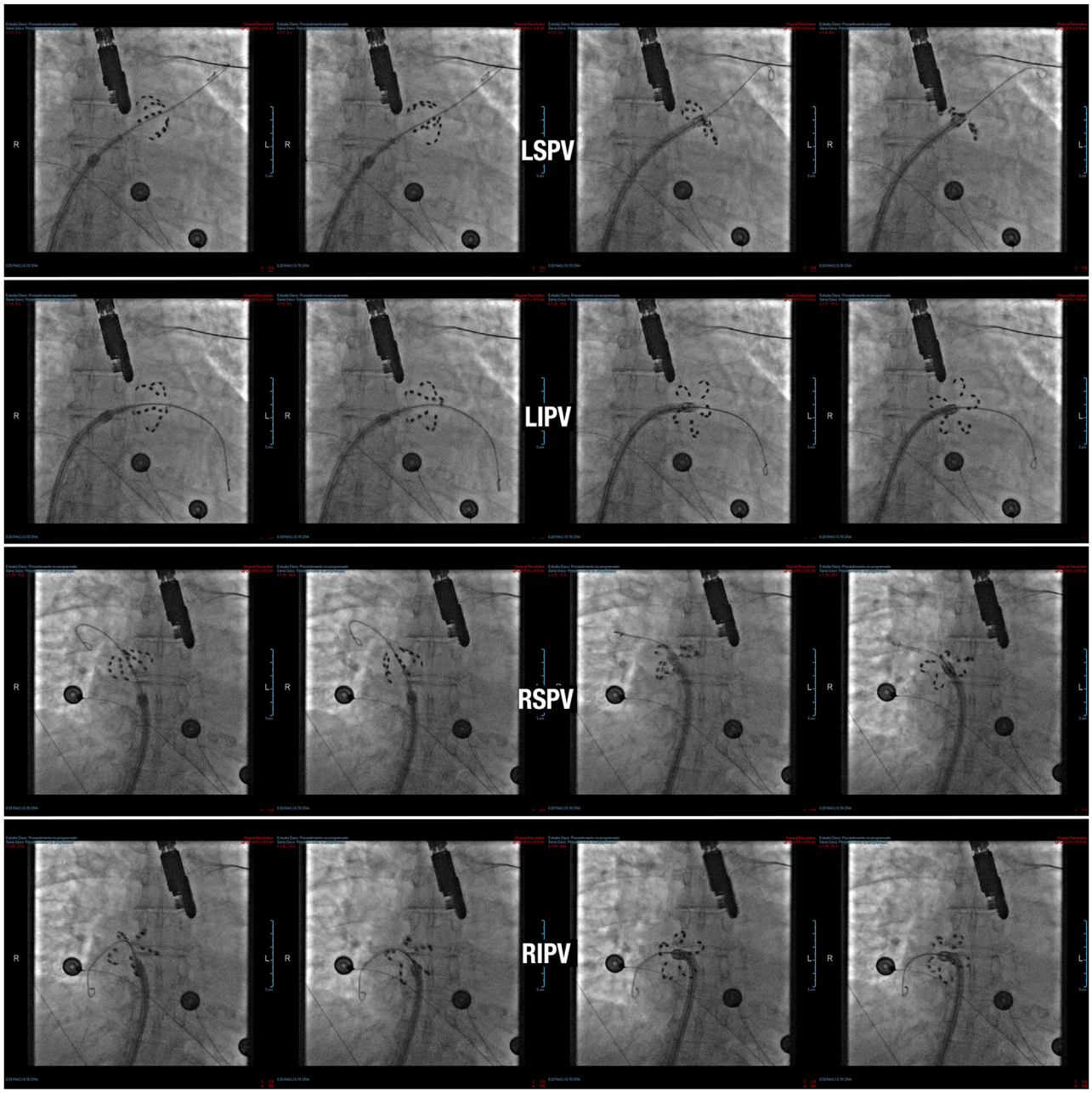

Figure 2 Standard protocol of energy applications. As previously described,[8,9] a total of 8 PFA lesions (voltage amplitude of 2.0 kV) were applied per vein: 4 each in "basket" and "flower" configurations, with rotation (halfway = 36°) between each pair of lesions. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PFA = pulsed field ablation; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

measured was 292 seconds. Using fluoroscopic guidance, a dedicated steerable sheath (Faradrive, Boston Scientific, Marlborough, MA) was introduced into the LA and, sequentially, an over-the-wire 31-mm PFA ablation catheter (Farawave, Boston Scientific). A previously described protocol of energy applications was delivered in each PV (Figures 2 and 3).[8,9] Additional applications were delivered at the operator's discretion to abolish local electrograms localized at either the carinas or PV antra. After 15 minutes, the ACT measured was 268 seconds. Timeline and additional procedure data are shown in Figure 4 and Table 1. Oral anticoagulation was resumed the evening after the procedure, and amiodarone treatment was withdrawn. The patient was discharged the next day with no complications and was asymptomatic in the 3-month follow-up visit.

Discussion

To the best of our knowledge, this is the first clinical report on the use of bivalirudin during a PFA-based ablation procedure. Owing to its immediate onset of action and short half-life (25 minutes),[1] bivalirudin is a well-established and

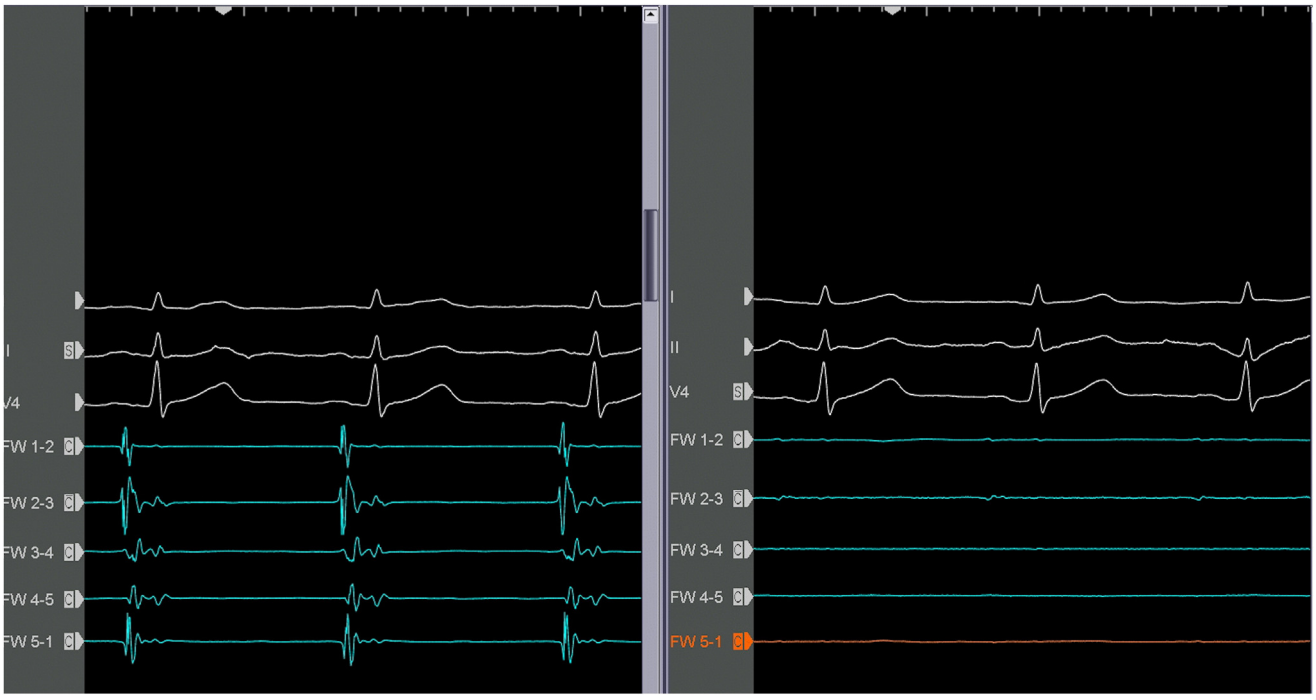

Figure 3 Example of acute abolition of PV electrograms after the first "basket" application in LPSV. PV = pulmonary vein; LSPV = left superior pulmonary vein.

evidence-based alternative to heparin in the setting of acute coronary syndromes undergoing percutaneous coronary interventions,[10,11] but there is no solid evidence regarding its use during ablation procedures. The largest study concerning the use of bivalirudin during catheter-based ablation procedures included 53 patients, of whom 34 (64%) underwent radiofrequency PVI for AF treatment.[12] The mean reported procedure time (including ventricular tachycardia substrates) was 216 minutes, with no reported complications among AF patients. The duration of our ablation procedure was 28 minutes, a much shorter time that goes in line of what is reported with the use of PFA compared with thermal ablation.[13]

Notably, in the previously mentioned study,[12] 43.5% of measured ACT levels were below the usual target of 350 seconds, a similar situation to what was observed in our case (268 seconds after 15 minutes). A well-known poor correlation among bivalirudin levels, activated partial thromboplastin time (aPTT), and ACT explains this finding and advises against their use to guide dosing. Bivalirudin's effect can be monitored using the aPTT test with a target aPTT ratio of 1.5–2.5 times the patient's baseline value. aPTT monitoring for bivalirudin has been more extensively used in the context of extracorporeal membrane oxygenation, in patients assisted with mechanical circulatory support, or for cardiopulmonary bypass during cardiac surgery. Nevertheless, depending on laboratory turnaround times, it might take too much time to get aPTT levels to monitor bivalirudin, particularly during short invasive procedures such as PFA-based PVI.

Finally, in a "real-world" setting of unselected AF population, PFA has already demonstrated a promising safety profile.[6] This may be not only explained by the intrinsic

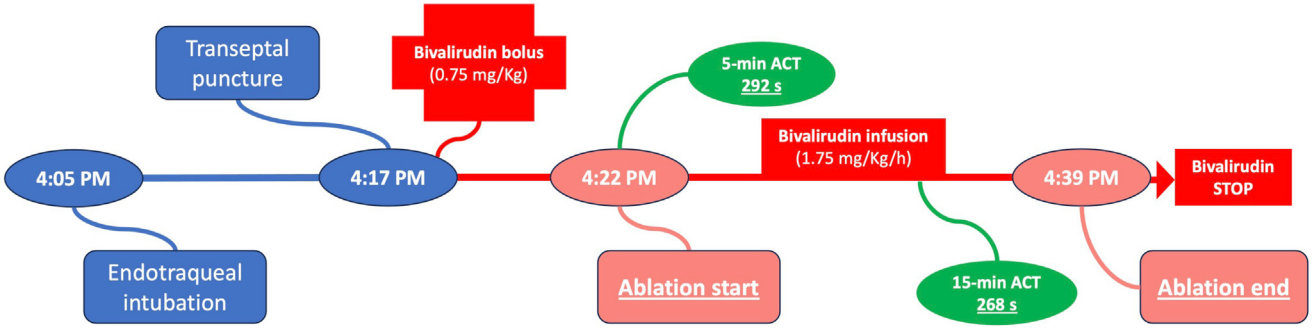

Figure 4 PFA-based PVI ablation procedure timeline. ACT = activated clotting time; PFA = pulsed field ablation; PVI = pulmonary vein isolation.

Table 1 Procedural data

	Time (min)
Total duration (skin to skin)	28
LA dwelling time	18
Total ablation time	17
LSPV ablation time*	4.5
LIPV ablation time*	4.5
RSPV ablation time*	4
RIPV ablation time*	4
Fluoroscopy time†	5.8
Bivalirudin infusion	22

LA = left atrial; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; PV = pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

*Ablation time per vein includes additional energy applications at the operator's discretion to fully cover PV antra (ie, anchoring applications). The total number of applications was 68.

†Total radiation dose: 44 mGy/4.18 Gy·cm^2.

myocardial tissue-selectivity of PFA but also through its correlation to shorter procedure times. Longer procedures have been associated with silent cerebral events (SLEs) during AF ablation.[14,15] In this context, the combination of PFA-based PVI procedures and the use of bivalirudin may provide a predictable safety profile. However, it should be acknowledged that SLE may still be detected in patients undergoing PFA-based PVI procedures. The prevalence of SLE may range from 0.09% to 8%,[16–18] depending on the studied population and the PFA device evaluated. Despite this, no relationship with symptomatic events has been able to be confirmed.[16–18] Thus, a potential limitation of the reported case might be the lack of postprocedural neuroimaging to rule out SLE after the use of bivalirudin. Moreover, intracardiac echo monitoring was unavailable, therefore making it difficult to rule out potential intraprocedural formation of thrombi.

Conclusion

Bivalirudin may be a useful and safe alternative to heparin during PFA-based PVI ablation procedures. Further studies evaluating its administration during ablation procedures using different PFA systems and manufacturers would be desirable. Systematic monitoring of these patients using intraprocedural intracardiac echo, and postprocedural neuroimaging could provide more evidence on the efficacy and safety of the reported strategy.

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