

## Ethanol Infusion in the Vein of Marshall in a Patient with Persistent Atrial Fibrillation

Jah Yeon Choi, MD, Eun Jin Park, MD, Hee Dong Kim, MD, Sung Hun Park, MD, Ji Young Song, MD, Dae In Lee, MD, Jaemin Shim, MD, and Young-Hoon Kim, MD

Department of Cardiology, Korea University College of Medicine, Anam Hospital, Seoul, Korea

We report the case of a 64-year-old male with persistent atrial fibrillation (AF) terminated by ethanol infusion into vein of Marshall as add-on therapy. Three-dimensional automated complex fractionated atrial electrogram (CFAE) during AF revealed clustering of CFAE at perimitral isthmus (PMI) and its unipolar mapping showed rotor-like activation, which was suggested to be critical in the perpetuation of AF. AF was organized to atrial tachycardia (AT) by 100% ethanol infusion in the vein of Marshall. Adjunctive radiofrequency ablation at PMI successfully terminated AT and led to bidirectional block of PMI. (**Korean Circ J 2015;45(5):424-427**)

**KEY WORDS:** Atrial fibrillation; Catheter ablation.

### Introduction

The vein of Marshall (VOM) is an embryonic remnant of the left superior vena cava.<sup>1)</sup> The ligament of Marshall (LOM), which contains nerves, fibrous tissues, and muscle bundles (Marshall bundle), is adjacent to the VOM.<sup>2)</sup> The LOM is a trigger of ectopic beats initiating paroxysmal atrial fibrillation (AF)<sup>3)</sup> and is innervated by the arrhythmogenic autonomic nerve.<sup>4)</sup> Moreover, the LOM is connected to the neighboring left atrium (LA) including the perimitral area and lateral ridge, and may be a part of the re-entrant circuit. Therefore, the LOM may play a role in the initiation and maintenance of AF or atrial tachycardia (AT). Recently, the feasibility of injection of pure ethanol into the VOM was demonstrated; the adjunctive effect to pulmonary vein isolation (PVI) was indicated.<sup>5)</sup> In addition, VOM

ethanol infusion assists in consisting achieving bidirectional perimitral isthmus (PMI) block.<sup>6)</sup> However, the effectiveness of the infusion in persistent atrial fibrillation (PeAF), which is an extensive substrate in the LA, is unclear. In the present case, AF was terminated by ethanol infusion adjunctive to complex fractionated atrial electrogram (CFAE) guided ablation in a patient with PeAF.

### Case

A 64-year-old male presented with a 6-month history of symptomatic drug refractory PeAF. The patient was admitted for catheter ablation of AF. Transthoracic echocardiogram revealed normal ejection fraction of 55–60% with mildly enlarged LA of 43.8 mm in the anterior-posterior diameter. A transesophageal echocardiogram prior to ablation showed no visible intracardiac thrombus or shunt. Cardiac magnetic resonance (CMR) imaging revealed late gadolinium enhancement (LGE) in 20% of the LA surface including the anterior and posterior wall.

After PVI, AF was still sustained. CFAEs in the LA were mapped for 6 seconds using EnSite NavX<sup>®</sup> system three-dimensional automated software (Endocardial Solutions, St. Jude Medical, St. Paul, MN, USA). The CFAEs were predominantly located at perimitral, septal area and left atrial appendage base (Fig. 1A and B). Activation pattern at the high clustering of CFAE was mapped using high density 20-pole catheters (AFocus II; St. Jude Medical, St. Paul, MN, USA). The activation patterns obtained from three AF beats of unipolar recordings at each CFAE site were classified into four categories: 1)

**Received:** September 28, 2014

**Revision Received:** October 16, 2014

**Accepted:** October 28, 2014

**Correspondence:** Young-Hoon Kim, MD, Department of Cardiology, Korea University College of Medicine, Anam Hospital, 73 Incheon-ro, Seongbuk-gu, Seoul 02841, Korea

Tel: 82-2-920-5211, Fax: 82-2-927-1478

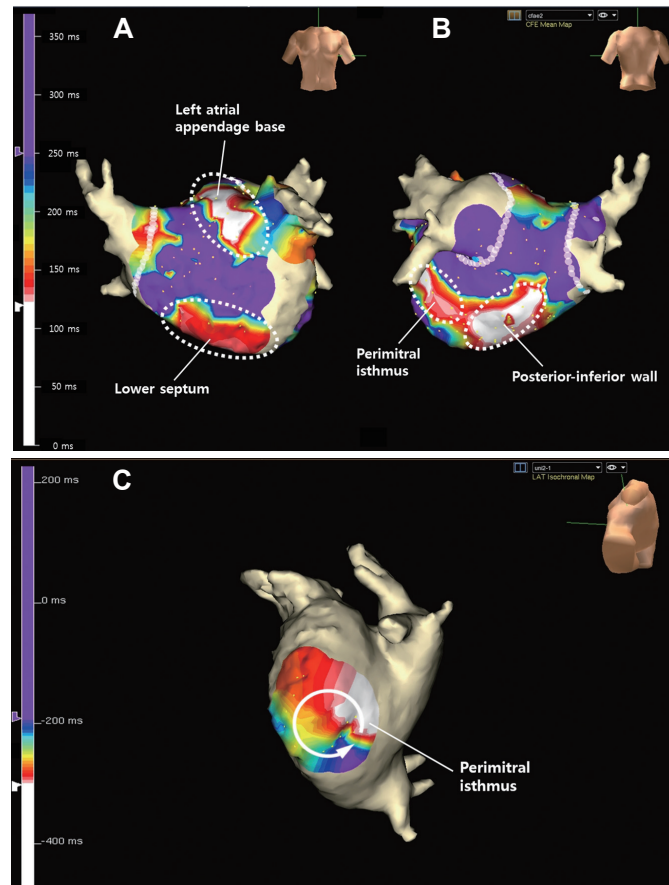
E-mail: yhkmd@unitel.co.kr

• The authors have no financial conflicts of interest.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

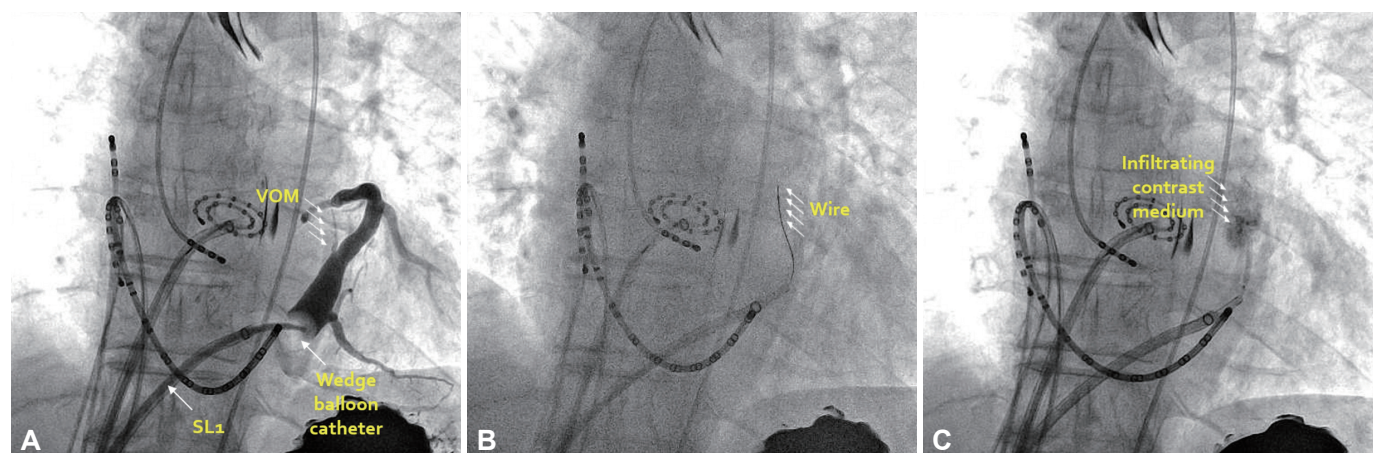
complete reentry, 2) incomplete reentry, 3) wave collision, and 4) wave breakup with conduction block. We preferentially targeted CFAE areas with complete or incomplete reentry pattern because

these sites might play an important role as rotor. In this case, only the perimitral area had re-entrant, rotor-like electrical activity (Fig. 1C). Based on the activation pattern, we assumed that the perimitral area could be the critical site for AF perpetuation. Therefore, we decided to infuse ethanol into the VOM as an add-on to radiofrequency ablation.

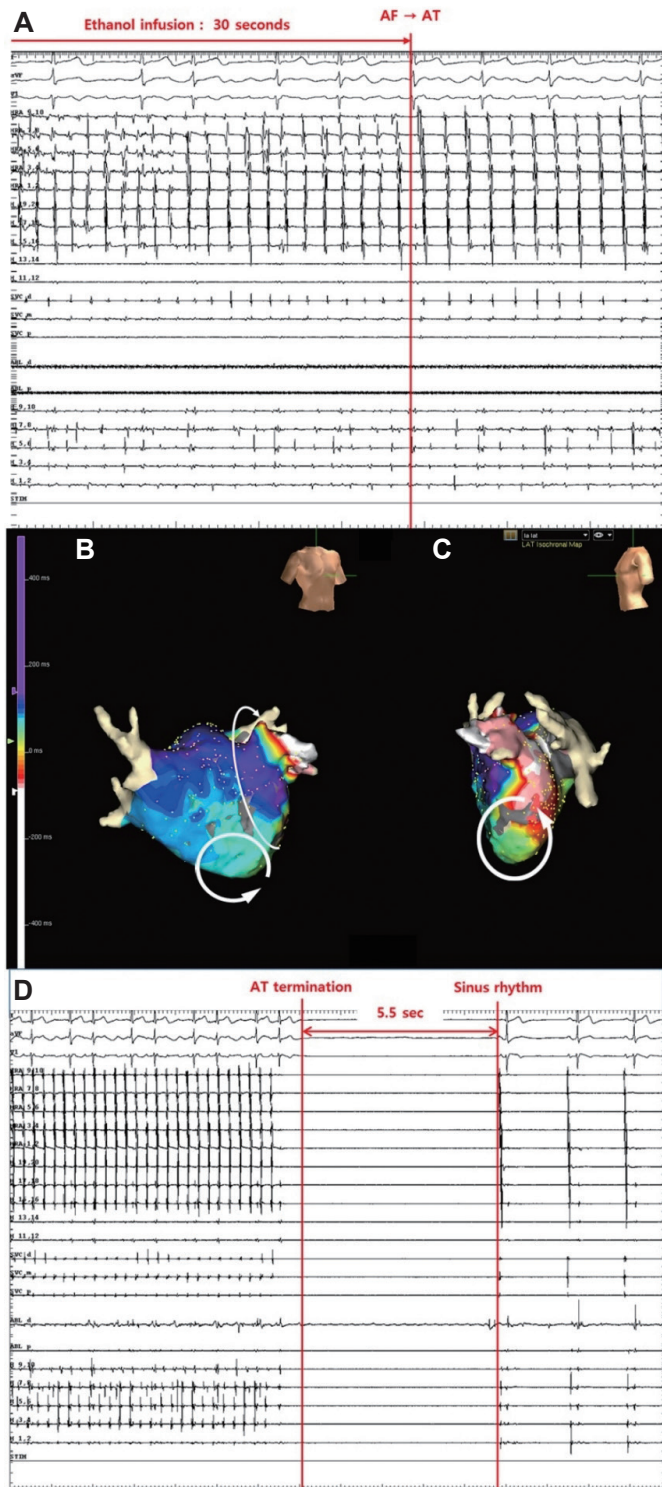


**Fig. 1.** CFAE mapping and unipolar mapping in LA after PVI. CFAE mapping (A and B) shows multiple CFAE areas which were located at LA septum, LAA base, PMI and posterior-inferior area. Unipolar mapping revealed reentrant atrial electrical activity at perimitral area (C). CFAE: complex fractionated atrial electrogram, LA: left atrium/left atrial, LAA: left atrial appendage, PVI: pulmonary vein isolation, PMI: perimitral isthmus.

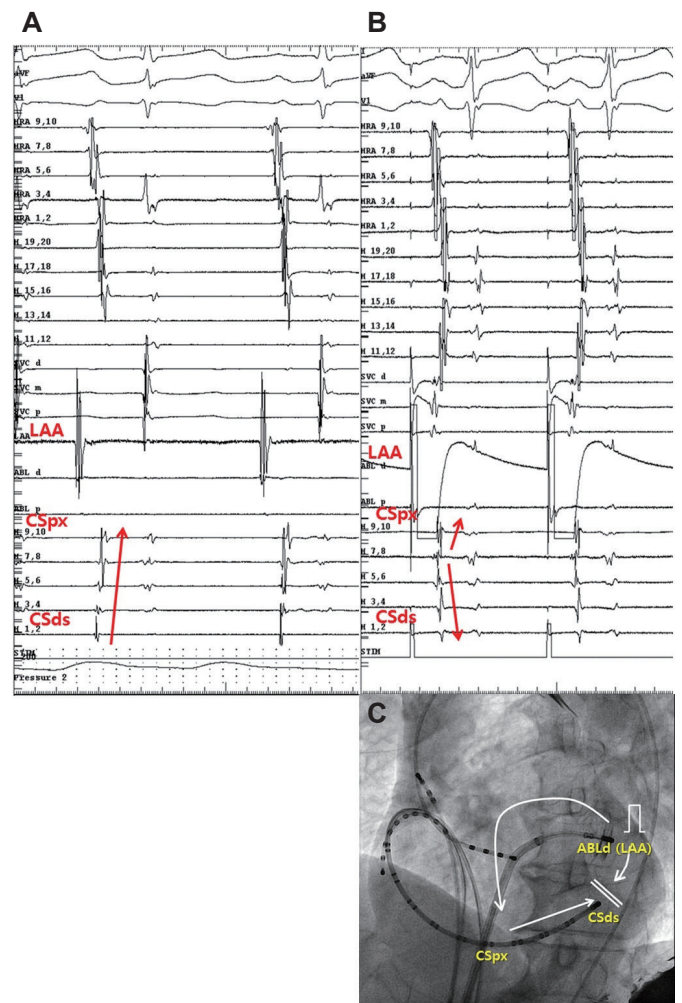
At first, cannulation into coronary sinus was performed by ablation catheter (Therapy CoolFlex; St. Jude Medical, St. Paul, MN, USA) and 8 Fr sheath (SL1 sheath; St. Jude Medical, St. Paul, MN, USA). To confirm the existence and feasibility of VOM, occlusive coronary sinus (CS) venogram was done (Fig. 2A). A multipurpose A-1 guiding catheter (7 Fr; Cordis, Miami, FL, USA) was subselectively engaged into the VOM and then a Hi-Torque Floppy II angioplastic guidewire 0.014 (Abbott, Santa Clara, CA, USA) was advanced into the VOM as far as possible. A Ryujiin Plus OTW 2.0x20 mm angioplasty balloon catheter (Terumo, Tokyo, Japan) was advanced into the VOM over the angioplastic wire and inflated at the ostium of VOM. Engagement of the balloon catheter into the VOM was confirmed by injecting contrast medium into the VOM (Fig. 2B), and 1 cc of 100% ethanol was injected into the VOM three times (Fig. 2C). Each injection was delivered over 1 minute through a balloon lumen and flushed with normal saline. Within 30 seconds after the first ethanol injection, AF was organized to AT (Fig. 3A). LA local activation time mapping demonstrated macro-reentrant AT, the circuit of which involved reentry around the mitral annulus in a counterclockwise fashion (Fig. 3B and C). Radiofrequency ablation at PMI for only 40 seconds terminated AT (Fig. 3D). Bidirectional block of PMI line was achieved after ablation within CS adjunct to PMI ablation (Fig. 4). The repeated induction test confirmed no inducibility. The patient has been followed at outpatient clinic without recurrence of AF/AT.



**Fig. 2.** Procedure of ethanol infusion into VOM. CS was cannulated by SL1 sheath and CS venogram using balloon catheter revealed VOM (A). Angioplastic wire (Hi-Torque Floppy II guidewire 0.014, Abbott) over guiding catheter (Multipurpose A-1 guiding catheter 7 Fr, Cordis) passed through VOM (B). After ethanol infusion, angiographic contrast was stained at the tissue around VOM (C). VOM: vein of Marshall, CS: coronary sinus.



**Fig. 3.** Electrogram changes during the procedure. Electrograms during ethanol infusion into VOM shows that AF was organized to AT within 30 seconds after first ethanol infusion (A). Activation mapping demonstrates the perimitral flutter (B and C). AT was terminated by endocardial ablation at perimitral isthmus (D). VOM: vein of Marshall, AF: atrial fibrillation, AT: atrial tachycardia.



**Fig. 4.** Conduction block achievement of PMI. During atrial premature complexes from LAA, CS electrogram shows distal to proximal activation (A). After ethanol injection into VOM with additional ablation at PMI, LAA pacing shows proximal to distal activation which means conduction block of PMI (B). The fluoroscopic image, left anterior oblique, showing position of ablation catheter and coronary catheter (C). PMI: perimitral isthmus, LAA: leftatrium appendage, CS: coronary sinus, VOM: vein of Marshall, CSpx: proximal part of coronary sinus catheter, CSds: distal part of coronary sinus catheter, ABLd: distal part of ablation catheter.

### Discussion

This case report demonstrates that ethanol infusion into the VOM can effectively eliminate CFAEs at PMI. In addition, we suggest that activation mapping at CFAEs area during AF can identify the critical CFAEs that maintain the PeAF. Even though the underlying etiology of CFAE has not been fully elucidated, CFAEs are considered as slow conduction or pivot sites, which represent continuous reentry of the fibrillatory waves.<sup>7)</sup> Based on these theories, CFAE guided ablation is widely used for modifying the extensive substrate of the LA and/or right atrium in patients with PeAF. However, whether CFAE reflects slow conduction or pivot site, or only wave collision that overlaps

different wavelets at the same area is contentious. Moreover, 90% of continuous CFAE sites do not overlap over LGE on CMR and occur at non-LGE and patchy LGE sites.<sup>8)</sup> Therefore, identification of the critical pivot site perpetuating AF among the continuous fractionated electrogram is necessary. In the present case, we performed unipolar activation mapping at the CFAE areas using a high density circular catheter to identify critical pivots and preferentially targeted the sites with complete or incomplete reentry pattern because these areas might be crucial for the perpetuation of AF. Among three CFAEs sites, only the PMI area had complete reentry pattern and ablation at this site easily lead to termination of AF. Therefore, this case suggests the usefulness of unipolar mapping to identify the true CFAE sites which is related to the persistence of AF. However, there is limitation of unipolar mapping, which includes difficulty in positioning the Lasso catheter at the LA septum, LA lateral ridge and below the LA appendage.

The present case highlights that PeAF can be terminated and organized to AT by ethanol infusion into the VOM. Valderrábano et al.<sup>5)</sup> demonstrated the feasibility of ethanol infusion into VOM adjunct to PVI; ethanol infusion decreased voltage around PMI and the LA lateral ridge. In addition, ethanol infusion in the VOM has an adjunctive effect in perimitral flutter ablation.<sup>6)</sup> The proximal portion of LOM has complex muscle fiber connections to CS adjacent to PMI.<sup>1)</sup> The mid-portion of LOM is directly connected to the LA lateral ridge and pulmonary veins.<sup>1)</sup> These muscle fiber connections can act as an anchor of re-entry. Therefore, ethanol infusion into the VOM can lead to substrate modification at PMI and LA lateral ridge. Moreover, the PMI area and LA lateral ridge are too thick to achieve transmural lesion only by endocardial ablation. Therefore, ethanol infusion in the VOM can be an effective intervention for achieving transmural scar and facilitating durable conduction block at this area. However, in this case, bidirectional block of PMI was not achieved by only ethanol infusion, but required endocardial PMI and intra-CS ablation adjunct to ethanol infusion. The transmural and

bidirectional block could be achieved by PMI ablation in only 15% of patients.<sup>9)</sup> This finding suggests that ablation of PMI concurrent with endocardial or epicardial lateral ridge may be needed to achieve transmural lesion in most cases. Therefore, ethanol infusion into VOM can be applied to the patients with PeAF, especially when CFAEs clusters at PMI area and the LA lateral ridge.

## References

1. Hwang C, Chen PS. Ligament of Marshall: why it is important for atrial fibrillation ablation. *Heart Rhythm* 2009;6(12 Suppl):S35-40.
2. Hsu LF, Jais P, Keane D, et al. Atrial fibrillation originating from persistent left superior vena cava. *Circulation* 2004;109:828-32.
3. Lin WS, Tai CT, Hsieh MH, et al. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. *Circulation* 2003;107:3176-83.
4. Kamanu S, Tan AY, Peter CT, Hwang C, Chen PS. Vein of Marshall activity during sustained atrial fibrillation. *J Cardiovasc Electrophysiol* 2006;17:839-46.
5. Valderrábano M, Liu X, Sasaridis C, Sidhu J, Little S, Khoury DS. Ethanol infusion in the vein of Marshall: adjunctive effects during ablation of atrial fibrillation. *Heart Rhythm* 2009;6:1552-8.
6. Báez-Escudero JL, Morales PF, Dave AS, et al. Ethanol infusion in the vein of Marshall facilitates mitral isthmus ablation. Ethanol infusion in the vein of Marshall facilitates mitral isthmus ablation. *Heart Rhythm* 2012;9:1207-15.
7. Nademanee K. Mapping of complex fractionated atrial electrograms as target sites for AF ablation. *Conf Proc IEEE Eng Med Biol Soc* 2011; 2011:5539-42.
8. Jadidi AS, Cochet H, Shah AJ, et al. Inverse relationship between fractionated electrograms and atrial fibrosis in persistent atrial fibrillation: combined magnetic resonance imaging and high-density mapping. *J Am Coll Cardiol* 2013;62:802-12.
9. Gaita F, Riccardi R, Caponi D, et al. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease: correlation of electroanatomic mapping and long-term clinical results. *Circulation* 2005;111:136-42.