

Atrial Fibrillation Ablation Using Vein of Marshall Ethanol Infusion

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ABSTRACT: Catheter ablation has become a cornerstone treatment for atrial fibrillation (AF). Pulmonary vein isolation is the accepted approach for paroxysmal AF ablation, but it is less effective for persistent AF. The vein of Marshall (VOM) is located in the epicardial left atrium and can be a source of AF triggers as well as a tract for autonomic nerves. It directly communicates with the underlying myocardium, including the left atrial ridge and the posterior mitral isthmus. This review discusses the latest evidence regarding the mechanisms, procedural aspects, and outcomes of VOM ethanol infusion when used as an adjunct to pulmonary vein isolation in patients with persistent AF.

INTRODUCTION

Catheter ablation is an essential component of the treatment of atrial fibrillation (AF). Pulmonary vein isolation (PVI) is the accepted procedural approach, based on the mechanistic idea that atrial extrasystoles originating from the pulmonary veins (PVs) trigger paroxysmal AF.¹⁻⁴ The mechanistic foundation is less clear in persistent AF, possibly more related to the chronic atrial substrate than to acute triggers from the PVs.⁵ This makes persistent AF ablation more challenging to treat, with less efficacious results than for paroxysmal AF.⁶ Although different substrate modification techniques have been attempted to improve outcomes—for example, creating linear lesions, ablation of complex fractionated atrial signals, isolation of the left atrial appendage, and others—these strategies remain controversial and not uniformly applied.¹

The ligament and vein of Marshall (VOM) appears to play a key role in atrial arrhythmogenesis, with an abundance of data supporting its electrical interaction with the PVs, its source of ectopic beats that trigger AF, and evidence of sympathetic and parasympathetic innervation.^{7,8} The VOM is located in the left atrial ridge and the posterior mitral isthmus, between the coronary sinus (CS) and the left inferior pulmonary vein,⁹ and can directly communicate with the underlying myocardium.^{10,11} Therapeutic approaches specifically targeting the ligament of Marshall had been limited to epicardial surgical ligation or sectioning of the ligament. The VOM is the continuation of Marshall's ligament. It is connected to the CS at the level of the valve of Vieussens and is amenable to selective retrograde cannulation.¹²

ETHANOL AS AN ABLATIVE AGENT

Zipes et al. were the first to deliver cytotoxic agents, in the form of alcohol, through vessels that target the myocardium.^{13,14} The most common alcohol used in these cases is ethanol, a highly

cytotoxic agent. Intravascular ethanol injections can create a chemical ablation in the targeted myocardial tissue by immediately decreasing the bipolar voltage in the endocardial aspect of ablated tissues, which sometimes will increase in size over the span of 10 to 15 minutes. The extent of low-voltage areas depends on the size of the VOM and its capillaries as well as the ethanol dose.

Ethanol infusion in the VOM was demonstrated to be feasible and efficacious in canines and later in human subjects.¹⁰ In humans, ethanol ablation of the VOM combined with radiofrequency ablation was synergistic in that it isolated the left PVs⁹ and eliminated the occasional direct ligament of Marshall-PV connections that may lead to reconnections and hinder the effect of AF ablation with PVI.^{1,15,16}

Baez-Escudero et al. showed that VOM ethanol infusion could effectively ablate the epicardial aspect of the left atrial ridge and the mitral isthmus and help eliminate perimitral flutter.¹⁷ In general, ethanol ablation is not sufficient to achieve perimitral block, and additional endocardial or epicardial radiofrequency may be required. Kawaguchi et al.¹⁸ found that mitral isthmus ablation and VOM ethanol infusion together could achieve a bidirectional conduction block at the mitral isthmus in approximately 93% of patients with an average of 4.8 minutes of RF application. They demonstrated that careful assessment of the CS atrial electrograms could predict conduction gaps and anticipate the need for additional RF applications in the CS.

PROCEDURAL ASPECTS

Ethanol injection in the VOM requires a blend of interventional cardiology and electrophysiology procedural skills, but it only requires a minor adaptation of workflow and tools commonly used for left ventricular lead delivery. One of the challenges is to understand the fluoroscopic anatomy of the VOM and its variants. However, carefully following the procedural steps can

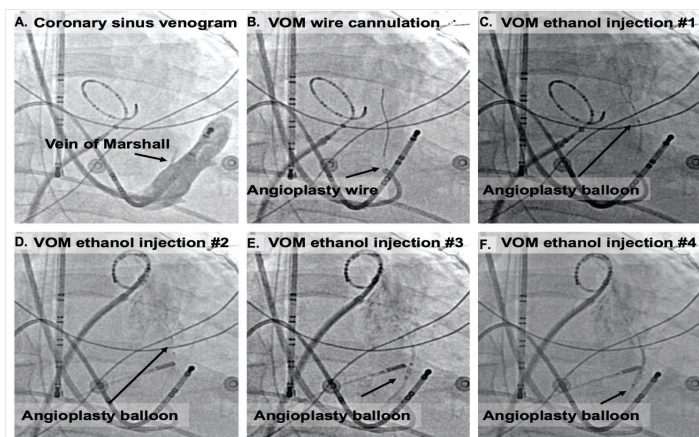


Figure 1.

Procedural steps for atrial fibrillation ablation using Vein of Marshall (VOM) ethanol infusion. (A) Coronary sinus (CS) venogram. From the internal jugular venous access, the CS is engaged with a sheath. Inside the CS sheath, a sub-selector left internal mammary artery (LIMA) guide catheter is inserted, and contrast is injected with the LIMA catheter tip pointing superiorly. The VOM is clearly visible via a nonselective injection through the LIMA. (B) Preloaded angioplasty wire and balloon are advanced into the VOM. Once the wire is securely engaged, the balloon is advanced as distally as possible in the VOM. (C-F) Balloon locations for the (C) first, (D) second, (E) third, and (F) fourth injection of ethanol in the VOM. Some myocardial staining occurs when contrast is injected after ethanol.

lead to a success rate of up to 89%, and failures can consistently be attributed to the anatomical absence of the VOM.

The first step in ethanol ablation is to cannulate the CS with an appropriate large sheath. The right internal jugular vein is our preferred access, but the left subclavian or femoral vein can be suitable as well. The next step is to assess whether the VOM is present or absent using direct contrast injection from the mid-CS with a subselector catheter or balloon occlusion CS venogram. The VOM can be recognized as a posteriorly directed branch of the CS (using a right-anterior oblique fluoroscopic projection) or as a superiorly directed branch. If the VOM is not immediately identified, adjustment of the catheter and/or the fluoroscopy view may be needed. Once identified, the next step is to cannulate the VOM using a left internal mammary artery angioplasty guide catheter or a sub-selective catheter for CS branch cannulation (for left ventricular lead delivery). In this step, the catheter tip is directed posteriorly while radiographic contrast is injected to confirm VOM engagement.

Once the catheter is engaged, the cannulation is secured by advancing the angioplasty wire as far as possible into the VOM. A preloaded over-the-wire angioplasty balloon (most commonly 6-mm length, 1.5-2 mm nominal diameter) is advanced into the VOM and inflated, and a selective VOM venogram is performed

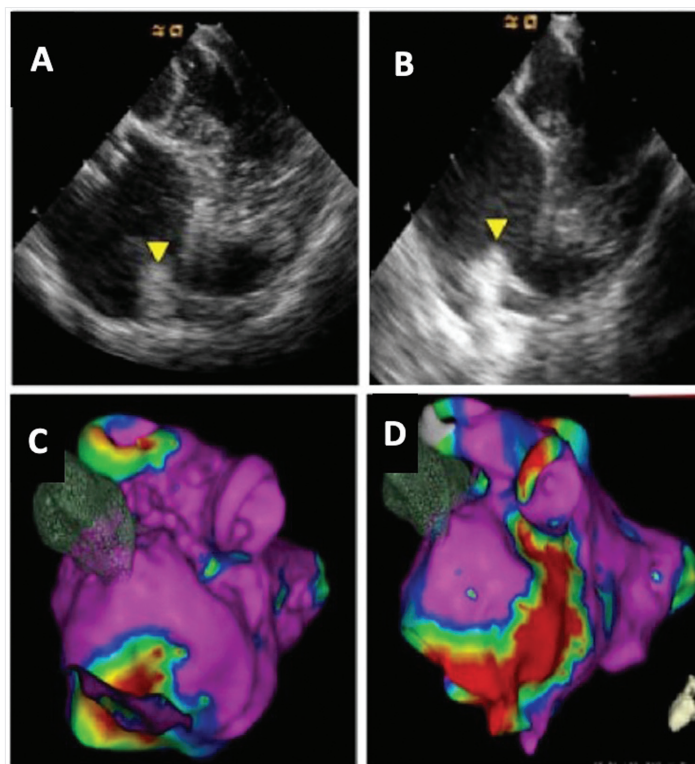
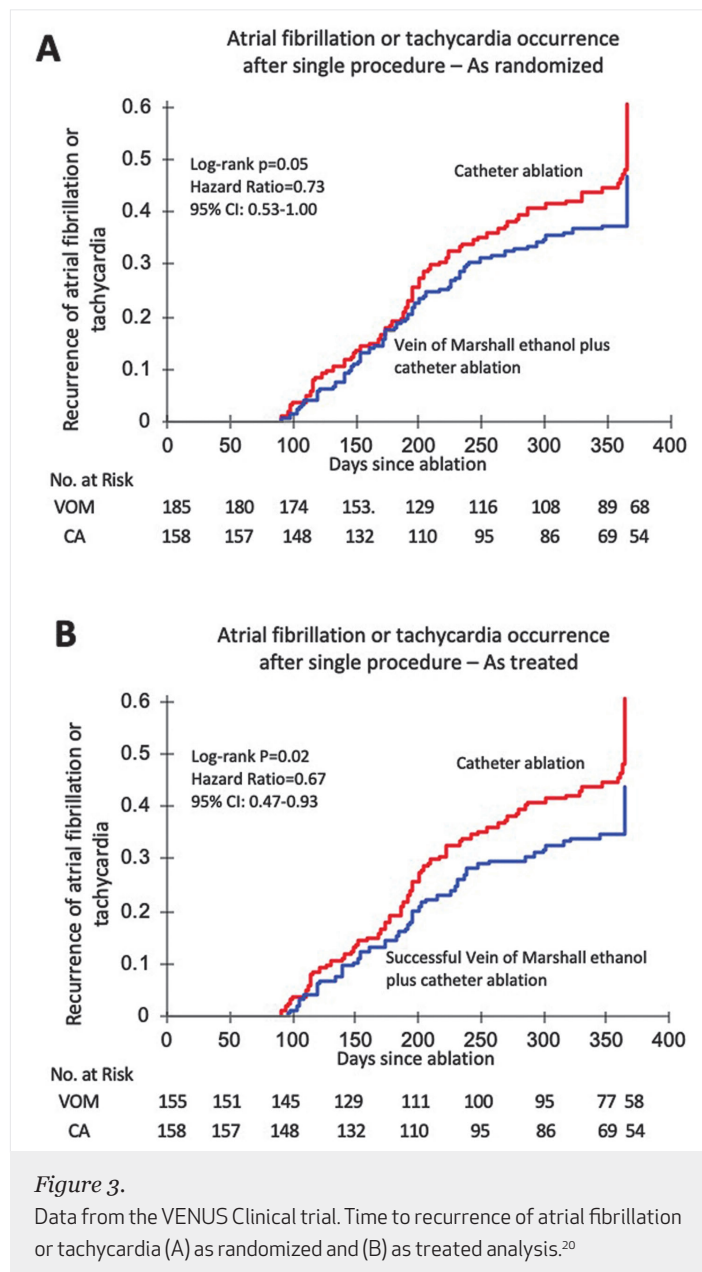


Figure 2.

Pre- and post-ethanol imaging demonstrating the scar created by Vein of Marshall (VOM) ethanol infusion using intracardiac echocardiogram imaging of (A, B) the left atrial ridge and (C, D) electroanatomical mapping.⁸

by injecting contrast into the balloon lumen. Ethanol is then infused into the VOM starting from the distal-to-proximal end. Once the first distal injection site is chosen, the balloon is inflated to between 2 and 4 atmospheres, although inflation can be omitted if contrast infusion already shows VOM occlusion. Once ethanol is delivered, the balloon is deflated, retracted 1 to 2 cm, and reinflated for subsequent ethanol delivery. Depending on the VOM's length, 2 to 4 separate injections of 1 cc 98% ethanol are administered over 2 minutes each and 2 minutes apart. Lastly, vein integrity is confirmed by repeat VOM angiograms (Figure 1).⁸ Ethanol will create a chemical ablation in the targeted myocardial tissue by causing an immediate decrease in bipolar voltage in the endocardial aspect of ablated tissues (Figure 2). The extent of low-voltage areas depends on the size of the VOM and its capillaries and the ethanol dose.¹¹ In general, a low-voltage scar can be mapped from the mitral annulus towards the left inferior pulmonary vein. Since this is the area of the posterior mitral isthmus, ethanol ablation can help achieve perimitral block and assist in treating perimitral flutter. Although this treatment leads to substantial ablation in this area, there may be gaps in the most annular aspect of the isthmus that require additional radiofrequency ablation.



OUTCOMES

Liu et al. recently published a retrospective series of three different ablation strategies for patients with nonparoxysmal AF, including PVI, substrate modification, or VOM ethanol infusion.¹⁹ Based on an average follow-up time of 3.9 years, VOM ethanol infusion was found to be an independent predictor of freedom from AF—validating the procedure's safety and feasibility and supporting its long-term efficacy. The series also suggests that VOM ethanol ablation improves AF ablation results for certain patients.

Valderrábano and colleagues recently published results from the VENUS trial (Vein of Marshall Ethanol Infusion for Persistent Atrial Fibrillation), a randomized controlled clinical trial that evaluated the therapeutic role of VOM ethanol ablation in treating persistent AF.^{20,21} A total of 343 patients were randomized to either catheter ablation alone ($n = 158$) or catheter ablation plus VOM ethanol infusion ($n = 185$). The primary end point was ablation success, defined as freedom from AF or atrial tachycardia longer than 30 seconds after a single procedure. By intention to treat, VOM ethanol ablation led to improved success of AF ablation (49.2% vs 38%, $P = .037$, OR 0.63, CI 0.41-0.97), and treatment differences were greater in a per-treatment analysis (51.6 % success, $P = .015$, OR 0.57, CI 0.37-0.90). Other end points—such as success after repeat procedures, AF burden, and need for repeat procedures—were similarly improved in the VOM ethanol ablation group. Figure 3 shows the trial design and outcomes.

RISK OF ETHANOL INJECTION IN THE VOM

Jugular vein access and additional CS instrumentation may lead to vascular damage. In the VENUS trial, however, the group receiving VOM ethanol ablation had no more significant vascular access complications compared to those receiving catheter ablation, and there was no difference in pericardial effusions, neither acutely during the procedure nor subacutely after the procedure. Patients undergoing VOM ablation tend to have more fluid overload post procedure than patients undergoing ablation with RF only, and diuresis should be considered.

CONCLUSIONS

VOM ethanol infusion is an effective method to create ablation in the mitral isthmus region and improve ablation success for persistent AF. Although it requires some familiarity with angioplasty tools and skills cannulating and navigating the coronary sinus, carefully following the aforementioned procedural steps can lead to consistent procedural success.

KEY POINTS

- The ligament and vein of Marshall (VOM) plays a key role in atrial arrhythmogenesis; it has electrical interaction with the pulmonary veins, it can be a source of ectopic beats that trigger atrial fibrillation (AF), and it contains autonomic nerves.
- VOM ethanol infusion is an effective method to create ablation in the mitral isthmus region.
- In patients with persistent AF, treatment with combined catheter ablation and VOM ethanol infusion improves ablation success.

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Conflict of Interest Disclosure:

The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

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