

# Electrical Isolation of the Marshall Bundle by Radiofrequency Catheter Ablation



## In Patients With Atrial Fibrillation

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### ABSTRACT

**OBJECTIVES** This study sought to isolate arrhythmogenic Marshall bundles (MBs) by radiofrequency (RF) catheter ablation.

**BACKGROUND** The vein of Marshall (VOM) is surrounded by a muscular bundle called the MB. The MB is 1 of the arrhythmogenic sources of atrial fibrillation (AF) and electrically connects to either the left atrial (LA) myocardium or coronary sinus (CS) musculature. By eliminating such electric connections using RF catheter ablation, the MB might be electrically isolated.

**METHODS** This retrospective study included 20 patients ( $64 \pm 10$  years old, 5 women) who underwent an MB isolation for nonparoxysmal AF. After pulmonary vein isolation, we performed venography of the VOM and inserted a 2-F electrode catheter into the VOM. RF applications were delivered to eliminate the MB electrograms from both the LA and CS when the MB was considered arrhythmogenic.

**RESULTS** MB isolation was achieved in 14 patients (70%). Of them, complete or partial MB isolation was accomplished in 7 patients (35%) each. The average number of RF applications in the LA (35 W, 30 s) and CS (25 W, 30 s) was  $15 \pm 14$  and  $4 \pm 3$ , respectively. No severe adverse events were observed. During a follow-up of  $23 \pm 11$  months, 18 patients (90%) maintained sinus rhythm.

**CONCLUSIONS** RF applications targeting recordings from an electrode catheter in the VOM were feasible, and the MB could be electrically isolated. Elimination of the MB potentials would be a clear endpoint for patients with an arrhythmogenic MB. (J Am Coll Cardiol EP 2020;6:1647-57) © 2020 by the American College of Cardiology Foundation.

The vein of Marshall (VOM) is a remnant of the left venous horn, which runs between the left pulmonary veins (PVs) and the appendage of the left atrium (LA) merging with the coronary sinus (CS). The VOM is coated or accompanied by a muscular bundle, the Marshall bundle (MB), which is known as 1 of the arrhythmogenic foci of atrial fibrillation (AF) (1). Interventions for the VOM have been performed using ethanol injections into the VOM (2) or radiofrequency (RF) ablation from the endocardium (3). Although the MB exists on

the epicardium and is considered to be insulated from the LA, there are electric connections either between the MB and LA myocardium or between the MB and CS musculature. Hence, it would be postulated that the MB could be electrically isolated if such electric connections were eliminated by RF applications. In fact, we previously reported the successful visualization of the partial isolation of the MB by RF applications (4). An electric MB isolation would be a clear endpoint for the isolation of an arrhythmogenic MB as an electric PV isolation, which is an established

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

Manuscript received February 4, 2020; revised manuscript received June 8, 2020, accepted June 23, 2020.

## ABBREVIATIONS AND ACRONYMS

**AF** = atrial fibrillation  
**AT** = atrial tachycardia  
**CFAE** = complex fractionated atrial electrogram  
**CL** = cycle length  
**CS** = coronary sinus  
**CTI** = cavotricuspid isthmus  
**LA** = left atrium  
**LAA** = left atrial appendage  
**LMI** = lateral mitral isthmus  
**MB** = Marshall bundle  
**PV** = pulmonary vein  
**RF** = radiofrequency  
**SR** = sinus rhythm  
**VOM** = vein of Marshall

endpoint of AF ablation. We attempted to electrically isolate the MB by RF applications and report the retrospective analysis.

## METHODS

**PATIENT SELECTION.** Between July 2015 and April 2018, catheter ablation of AF was conducted in 732 patients including 261 patients with nonparoxysmal AF at Keio University Hospital. The patients underwent 190 first sessions, 52 second sessions, 15 third sessions, 3 fourth sessions, and 1 fifth session. The indication for AF catheter ablation was based on the Japanese guidelines of nonpharmacological therapy for cardiac arrhythmias (5). All of the patients underwent a PV isolation with box lesion sets and the simultaneous isolation of all 4 PVs and the LA

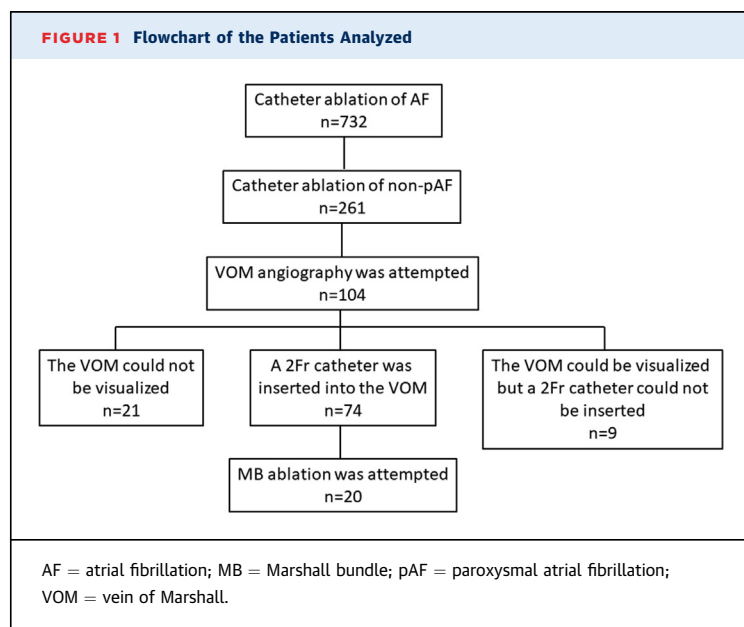
posterior wall. Subsequently, we performed MB isolation in 20 selected patients. This study was approved by our Institutional Review Board based on the ethical guidelines of the Declaration of Helsinki. All patients provided informed consent before the catheter ablation.

**CATHETER ABLATION.** Oral anticoagulation therapy with warfarin given within the therapeutic range or with direct oral anticoagulants was introduced at least 1 month before the ablation procedure. All antiarrhythmic drugs were discontinued for at least 5 half-lives before the ablation. Within a few days before the ablation, we performed

transesophageal echocardiography to rule out any thrombus formation in the left atrial appendage (LAA) and cardiac computed tomography to create a 3-dimensional LA geometry for the 3-dimensional mapping system.

Catheter ablation of AF was performed under deep sedation. An esophageal temperature probe (Sensi-Therm, St. Jude Medical, St. Paul, Minnesota) was introduced from the nasal cavity (6). A 6-F, 14 wide band electrode catheter (Inquiry) was inserted into the CS through the right jugular vein, which covered the CS and lateral RA region and was also used for intracardiac direct current cardioversion. A 6-F quadripolar electrode catheter (Inquiry) was positioned in the right ventricular apex through the femoral vein. Three long sheaths, 1 a steerable sheath (Agilis, St. Jude Medical) for the ablation catheter and the others nonsteerable sheaths (SLO and SL1, Swartz, St. Jude Medical) for the ring electrode catheters, were advanced into the LA. A box isolation with single linear lesions encircling all 4 PVs and the LA posterior wall was performed using a 3-dimensional electroanatomic mapping system with an irrigated-tip catheter (Thermocool Smarttouch SF, Biosense Webster, Diamond Bar, California) and validated with 2-ring electrode catheters (Lasso 2515 NAV Eco Catheter, Biosense Webster, and Inquiry A Focus, St. Jude Medical) inserted through long sheaths, which were positioned on both PV sides. The encircling linear lesions were created in a point-by-point manner with 30-s RF applications at each point. The output was set at 30 to 35 W with an irrigation flow of 17 to 30 ml/min, which was decreased to 20 to 25 W with a flow of 17 ml/min near the esophagus. The alarm of the esophageal temperature system was set at 38°C, at which point the RF power was switched off (6). The endpoint of the box isolation was the elimination of dormant conduction revealed by a 20-mg adenosine triphosphate infusion. An intracardiac direct current cardioversion was applied using CS catheter electrodes when AF still persisted after the box isolation. Subsequently, a cavotricuspid isthmus (CTI) ablation with or without a lateral mitral isthmus (LMI) ablation was appended according to the physicians' discretion. RF energy was also delivered for non-PV triggers or atrial tachycardias (ATs) that were repeatedly induced by programmed electric stimulation with or without an infusion of isoproterenol. Moreover, RF ablation targeting complex fractionated atrial electrograms (CFAEs) could be performed, especially in patients with a redo ablation. The arrhythmogenicity of the MB was evaluated by inserting a 2-F catheter into the VOM at the time of the completion of the PV isolation during AF or during the restoration of sinus

**FIGURE 1** Flowchart of the Patients Analyzed



**TABLE 1 Patient Characteristics of the Marshall Bundle Isolation**

Patient #	Age (yrs)	Sex	Type	LA (mm)	Prior Ablation	Concomitant Procedures
1	76	M	ls-per AF	44	PVI, CTI, SVCI, LA CFAE	SVCI, LA/RA CFAE, Roof, Bottom, LMI
2	70	F	ls-per AF	56		Box, LMI, LA CFAE
3	68	F	ls-per AF	39		Box, CTI, LMI
4	70	M	ls-per AF	49		Box, CTI, LMI
5	73	M	ls-per AF	50		Box, CTI
6	69	M	per AF	41	PVI, Roof, Bottom, CTI, LMI	LA/RA CFAE, LMI
7	75	M	per AF	39	PVI, CTI	Roof, Bottom, CTI, LMI, RA CFAE
8	48	M	AT	42	Box, CTI, LMI	PVI, Roof, LMI, CS
9	70	M	ls-per AF	34		Box, CTI
10	66	M	ls-per AF	39		Box, CTI, LMI
11	62	M	ls-per AF	36		Box, CTI, LMI
12	57	F	ls-per AF	46		Box, CTI, LMI
13	53	M	ls-per AF	35		Box, CTI, LMI
14	70	M	ls-per AF	48		Box, CTI
15	36	M	per AF	28	PVI, LA/RA CFAE	SVCI, CTI
16	64	M	ls-per AF	55		Box, CTI, LMI
17	61	F	per AF	41	PVI	LMI, CS CFAE
18	68	M	ls-per AF	39		Box, CTI
19	72	F	ls-per AF	45		Box, CTI, LMI
20	51	M	ls-per AF	41		Box, CTI, LMI
64 ± 10		75%	80%	42 ± 7		

Values are mean ± SD or n (%).

AT = atrial tachycardia; Bottom = bottom line; Box = box isolation; CFAE = complex fractionated atrial electrogram; CS = coronary sinus; CTI = cavotricuspid isthmus line; LA = left atrium; LMI = left mitral isthmus line; ls-per AF = longstanding persistent atrial fibrillation; PVI = pulmonary vein isolation; RA = right atrium; Roof = roof line; SVCI = superior vena cava isolation.

rhythm (SR) by cardioversion. Furthermore, the intervention for the MB as described later was performed during or after the previously mentioned ablation procedures.

**MB ABLATION.** Arrhythmogenicity of the MB was suspected: 1) when the cycle length (CL) of the local activation was the shortest recorded on the CS electrodes during persistent AF after the box isolation; or 2) if atrial premature contractions were observed from the CS, especially from the midportion during SR after a cardioversion because the MB was considered to be connected to the CS musculature. In such situations, 1 of the SL sheaths was pulled back to the RA after pulling out the ring electrode catheter, and a 6-F multipurpose catheter (CX catheter, Gadellius Medical, Tokyo, Japan) was inserted into the SL sheath instead; CS venography using a multipurpose catheter was obtained. If a VOM was observed, a 2-F octapolar electrode catheter (EP star Fix, Japan Lifeline, Tokyo, Japan) was advanced into the VOM as deeply as possible through the multipurpose catheter.

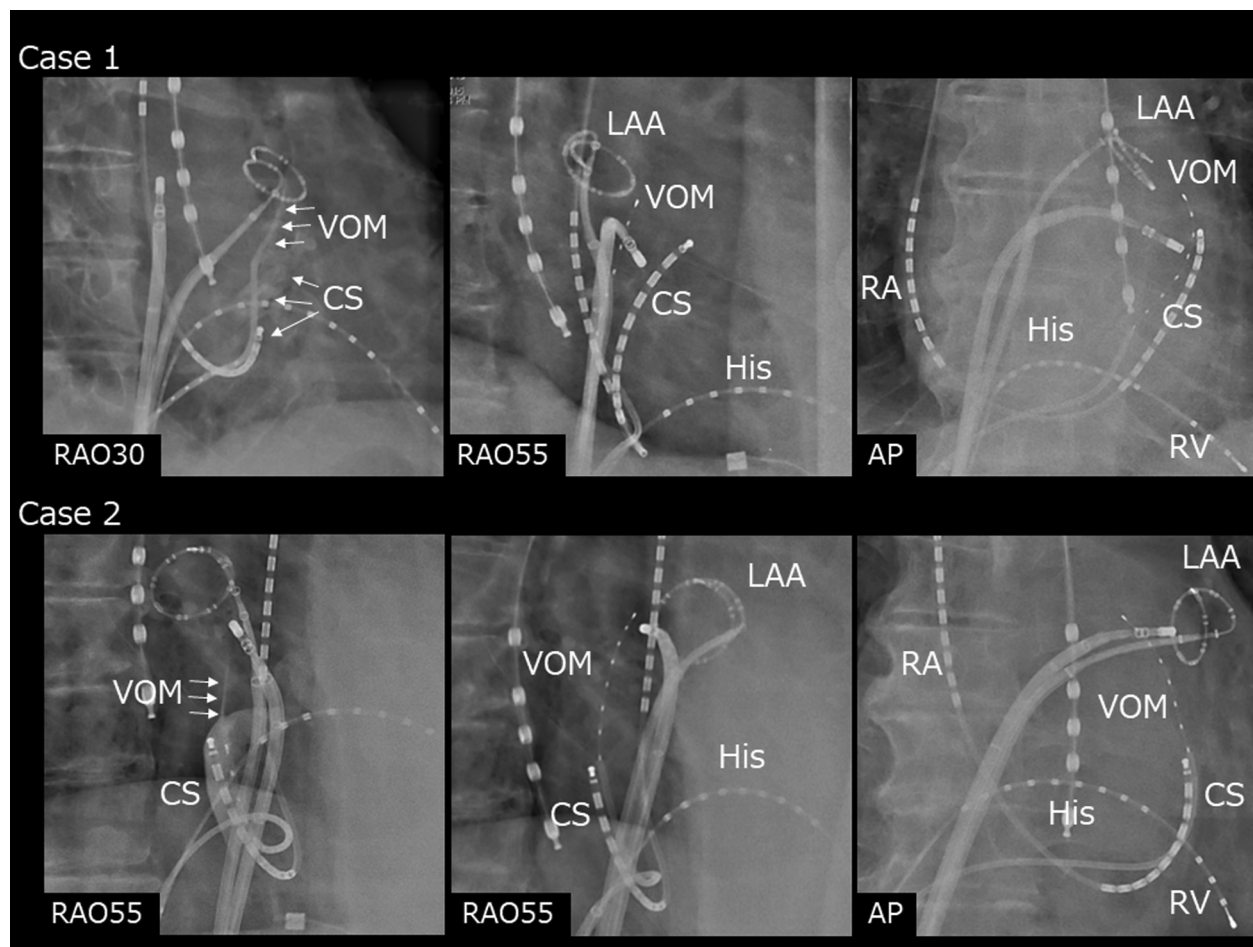
RF applications were delivered repeatedly in a point-by-point manner to eliminate the MB

electrograms from both the LA endocardium at 35 W for 30 s and the CS at 25 W for 30 s. For the endocardial ablation, RF energy was applied mainly targeting the VOM electrodes along the entire VOM electrode catheter. For the ablation from the CS, the RF energy was delivered around the branching portion of the VOM from the CS. The electric isolation of the MB was confirmed by a bidirectional block of the MB during SR. The definition of a complete isolation of the MB was the elimination of all electrograms recorded by the 2-F catheter electrodes inserted into the VOM. A partial isolation of the MB was defined as the elimination of a part of the MB electrograms.

**FOLLOW-UP.** After discharge, a portable electrocardiogram (Cardiophone, Nihon Kohden, Inc., Tokyo, Japan) was used to detect any recurrence of atrial tachyarrhythmias in all patients for the first 6 months; patients sent electrocardiograms routinely 2 times per day and each time when having arrhythmic symptoms. A 24-h Holter electrocardiogram was performed every 6 months.

**STATISTICAL ANALYSIS.** Continuous variables were presented as the mean ± SD or the median

**FIGURE 2** Venography and Catheter Placement in the Clinical Cases



The **left upper panel** shows the venography in case 1 in which the multipurpose catheter was directly cannulated into the vein of Marshall. The **left lower panel** shows the coronary sinus venography in case 2. In this particular case, the coronary sinus was angulated acutely anteriorly at the bifurcation of the vein of Marshall, and the coronary sinus catheter could not be advanced from that point. AP = anterior-posterior; CS = coronary sinus; CS-d = distal coronary sinus; CS-p = proximal coronary sinus; HBE = His bundle electrogram; His = His bundle; LAA = left atrial appendage; RA = right atrium; RAO = right anterior oblique; RV = right ventricle; VOM = vein of Marshall; VOM-d = distal vein of Marshall; VOM-p = proximal vein of Marshall.

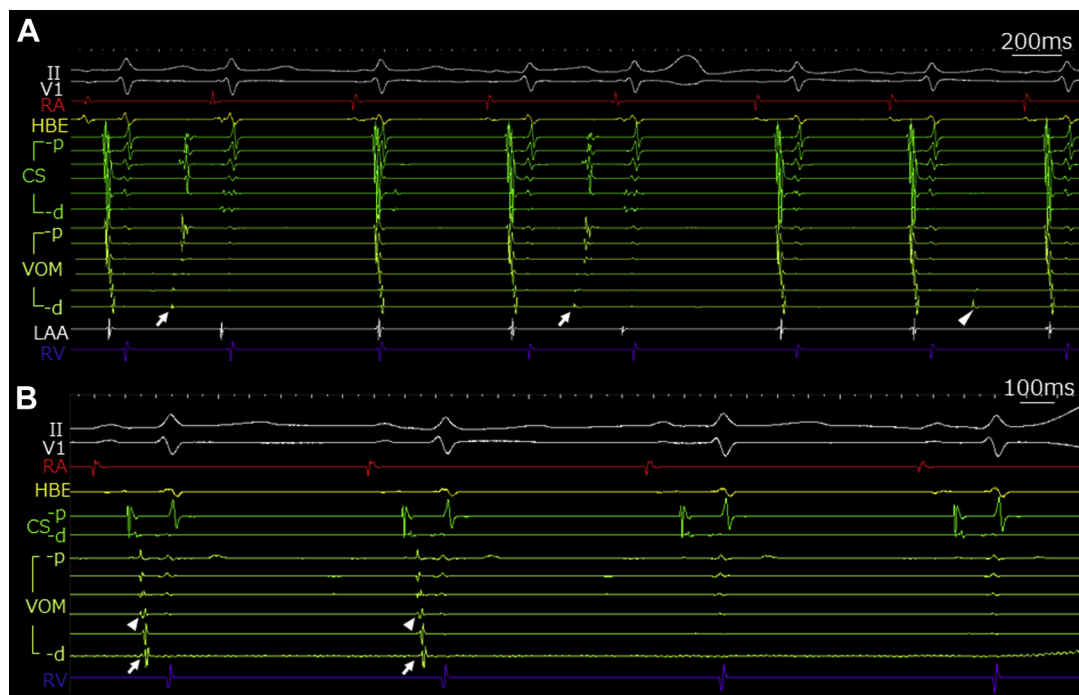
(interquartile range). Categorical data were presented as numbers and percentages. The Kruskal-Wallis test and a nonparametric multiple comparison (Steel-Dwass test) were used to compare the differences across groups, including the complete isolation, partial isolation, and failure group. These tests were also used to compare the differences among the CLs of the VOM, LAA, and CS. The Mann-Whitney *U* test was used to compare the differences in the CLs and amplitude of the MB potentials before and after the MB ablation. A *p* value < 0.05 was considered to indicate statistical significance. These analyses were performed using EZR software (Saitama

Medical Center, Jichi Medical University, Saitama, Japan).

## RESULTS

**PATIENT CHARACTERISTICS.** Among 261 consecutive nonparoxysmal AF patients who underwent catheter ablation, CS venography was performed in 104 patients. Of them, the VOM could not be visualized in 21 patients, and the size of the VOM was too small to insert a 2-F catheter in 9 patients. Hence, the insertion of the 2-F catheter into the VOM was successfully achieved in 74 patients. Of them, we

**FIGURE 3 Complete Isolation of the Marshall Bundle Potentials**



**(A)** Arrhythmogenicity of the Marshall bundle during sinus rhythm. Ectopies from the distal vein of Marshall (arrows, arrowhead) were observed. The third ectopy from the distal vein of Marshall (arrowhead) did not conduct to the left atrium or coronary sinus and was considered to represent functional conduction block in the Marshall bundle. In this particular case, a radiofrequency application in the mitral isthmus region was applied, which affected the conduction of the Marshall bundle. **(B)** Complete isolation of the Marshall bundle. The Marshall bundle potentials (arrows, arrowheads) were completely isolated by radiofrequency applications from both the left atrial endocardium and coronary sinus during sinus rhythm. Abbreviations as in Figure 2.

attempted to ablate the MB in 20 patients whose MB was considered arrhythmogenic (Figure 1), whereas the MB was considered to be a bystander in the remaining 54 patients. The background is shown in Table 1. The mean age was 64 years, and 15 patients (75%) were male. The mean LA diameter was 42 mm. The study population included 15 (75%) long-standing persistent AF patients and 6 with a history of a prior catheter ablation. All patients, except for Patients #15 and #17, underwent a simultaneous isolation of the PV and LA posterior wall, and the concomitant ablation procedures are summarized in Table 1. An LMI linear ablation was attempted and achieved in 10 patients (50%) before the MB ablation and in 5 patients (25%) after the MB isolation, and it was not applied in the remaining 5 patients.

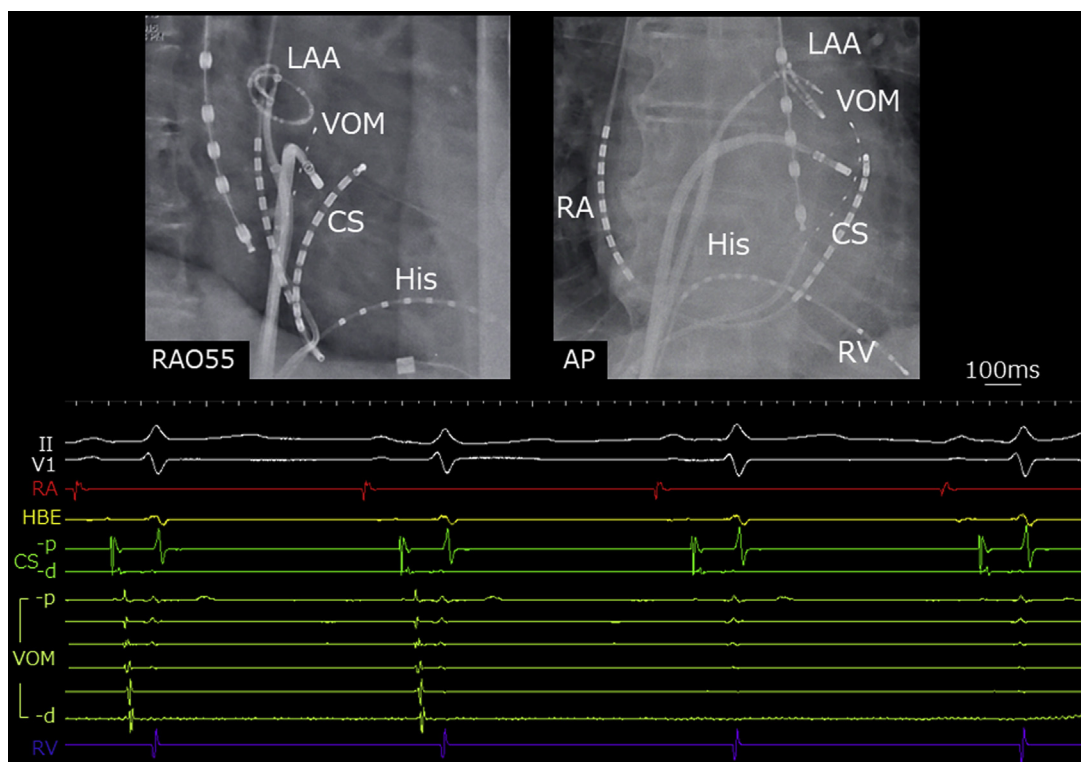
Among 20 patients, 14 had significantly shorter CLs in the VOM than in the LAA and CS during AF, and the CLs in the VOM, LAA, and CS were  $133 \pm 29$  ms,  $160 \pm 21$  ms, and  $166 \pm 33$  ms, respectively ( $p < 0.001$ ). On the other hand, 6 patients had ectopic activity

originating from the VOM during SR, and the coupling intervals were  $254 \pm 18$  ms and  $817 \pm 200$  ms during SR with CLs of  $482 \pm 92$  ms and  $1,272 \pm 167$  ms with and without isoproterenol, respectively. As a result, the MB ablation was performed during SR, AF, and AT in 11, 6, and 3 patients, respectively, because 9 of 14 AF patients had SR restored by cardioversion and 2 of them developed AT before the MB ablation and 1 out of 6 SR patients developed AF and AT before the MB ablation.

**REPRESENTATIVE CASES.** Patient# 6 (case 1) was a 69-year-old man with persistent AF (CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2) whose LA diameter was 41 mm. The PV isolation was performed by RF, and LA roof and bottom lines, a CTI line, and an LMI line were created; however, recurrent persistent AF was observed. In the second session, after the confirmation of the isolation of all PVs, RF ablation targeting CFAEs in the LA and RA was performed. Subsequently, after cardioversion to SR, because the LMI line was



# **CENTRAL ILLUSTRATION** Electric Isolation of the Marshall Bundle



Kashimura, S. et al. J Am Coll Cardiol EP. 2020;6(13):1647-57.

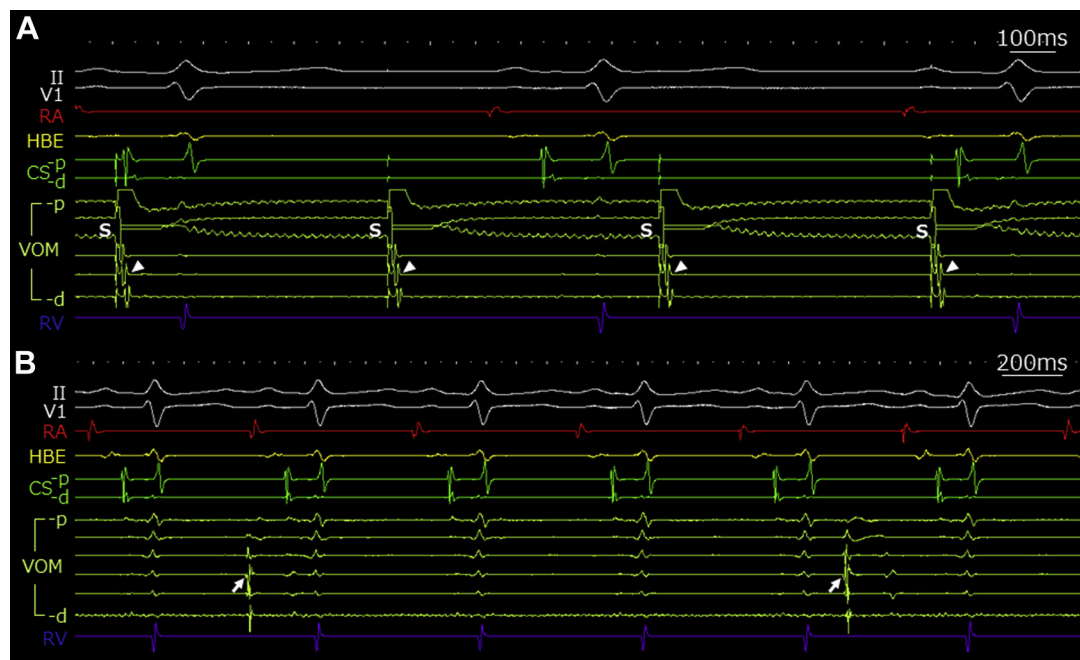
The Marshall bundle potentials were completely isolated by radiofrequency applications from both the left atrial endocardium and the coronary sinus during the sinus rhythm. AP = anterior-posterior; CS = coronary sinus; CS-d = distal coronary sinus; CS-p = proximal coronary sinus; HBE = His bundle electrogram; His = His bundle; LAA = left atrial appendage; RA = right atrium; RAO = right anterior oblique; RV = right ventricle; VOM = vein of Marshall; VOM-d = distal vein of Marshall; VOM-p = proximal vein of Marshall.

incomplete, a bidirectional LMI block was recreated by RF applications. With an isoproterenol infusion, frequent ectopies from the CS were observed. A 2-F electrode catheter was inserted into the VOM (Figure 2, upper panels), which revealed that the ectopies originated from the distal VOM (Figure 3A). MB isolation was conducted, and the RF delivery from the LA and CS isolated the MB electrograms (Figure 3B), Central Illustration. All of the electrograms from the VOM electrodes were eliminated in this case, which represented the complete isolation of the MB. After the isolation, pacing from the VOM electrodes revealed the local capture of the MB, which did not conduct to the LA, confirming the exit block (Figure 4A). The isoproterenol infusion provoked automatic activity from the MB (Figure 4B). The RF delivery points for the MB isolation are shown in the CARTO image (CARTO, Biosense Webster, Inc., Irvine,

California) in the upper panels of Figure 5, which are distributed within the posterolateral LA connecting the CS and the ridge of the left PV at the level of the left inferior PV.

Patient #1 (case 2) was a 76-year-old patient with long-standing persistent AF (CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 2) whose LA diameter was 44 mm. An ipsilateral PV isolation and CTI ablation were performed in the first session. Persistent AF recurred and a reisolation of the PVs, isolation of the superior vena cava, and CFAE ablation in the LA were performed in the second session. However, persistent AF recurred, and the patient underwent a third session. After the confirmation of the isolation of all PVs, the LA roof and bottom lines were created, and CFAE ablation in the LA was performed. Next, the VOM electrode catheter was inserted (Figure 2, lower panels). The CLs of the VOM were shorter than those of the CS and LAA

**FIGURE 4** Bidirectional Block Between the Marshall Bundle and the Left Atrium



(A) Confirmation of the exit block of the Marshall bundle. Electric stimulation was used in the mid of the vein of Marshall to capture the Marshall bundle potentials through the electrodes (arrowheads). The activation did not conduct to the left atrium or the coronary sinus. (B) the automatic activity of the Marshall bundle. Marshall bundle automaticity (arrows) emerged after an isoproterenol infusion during sinus rhythm. S = stimulation; other abbreviations as in Figures 1 and 2.

during AF, which indicated the arrhythmogenicity of the MB (Figure 6A). The RF energy delivered from both the LA and CS targeting the VOM catheter isolated the MB electrograms (Figure 6B). The electrograms recorded by the midpart to the distal part of the VOM electrodes were eliminated. However, those of the proximal part still remained, which represented a partial isolation of the MB. The lower panels of Figure 5 indicate the RF delivery points for the MB isolation.

**MB ISOLATION.** Of 20 patients, 7 (35%) had a complete or partial MB isolation each. Notably, it resulted in a failure in 6 patients (30%). Automatic activity from the isolated MB was observed in 3 patients (21%) after the ablation. The MB potentials were recorded by  $7 \pm 1$  electrodes of the VOM catheter, and the average amplitude before the MB ablation was  $1.6 \pm 1.2$  mV. For the MB isolation, the average cumulative RF energy was  $16,119 \pm 15,371$  J. The average number and duration of the RF deliveries in the LA ( $n = 20$ ) and CS ( $n = 16$ ) were  $15 \pm 14$  and  $4 \pm 3$  and  $391 \pm 396$  s and  $94 \pm 90$  s, respectively. The average total procedure time was  $254 \pm 72$  min, the average total

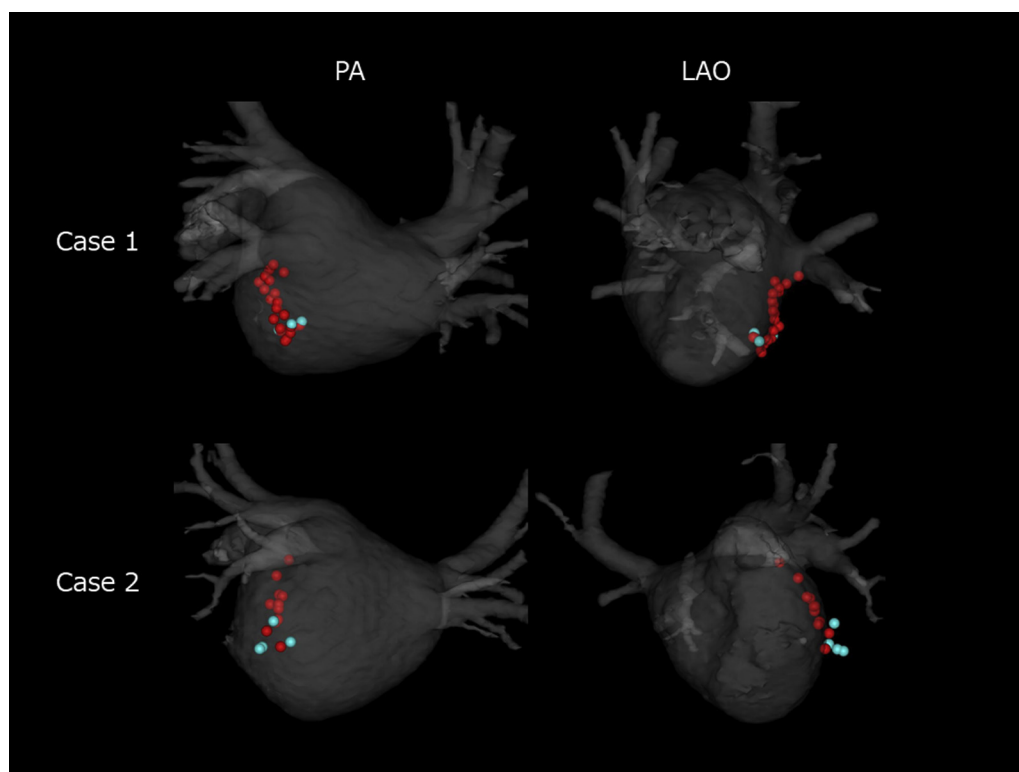
fluoroscopic time  $45 \pm 14$  min, and average total radiation dose  $350 \pm 229$  mGy.

In the complete isolation group ( $n = 7$ ), the amplitude of the MB potentials before ablation was  $2.1 \pm 1.5$  mV, and the CL of the VOM electrograms during AF before the ablation was  $102 \pm 11$  ms. In the partial isolation group ( $n = 7$ ), the amplitude of the MB potentials before and after the ablation was  $1.5 \pm 1.0$  mV and  $0.7 \pm 0.8$  mV ( $p < 0.01$ ), and the CL of the VOM electrograms during AF before and after the ablation was  $122 \pm 18$  ms and  $182 \pm 38$  ms, respectively ( $p < 0.001$ ). In the failure group ( $n = 6$ ), the amplitude of the MB potentials before and after the ablation was  $1.2 \pm 0.9$  mV and  $0.8 \pm 0.5$  mV (not significant).

A comparison of these 3 groups is depicted in Table 2. The failure group required a significantly higher delivered energy, number of RF applications, and a longer time to isolate the MB from the LA.

The intervention for the MB was performed without any adverse events. During a follow-up of  $23 \pm 11$  months, 18 patients (90%) maintained SR. AF recurred in 2 patients (Patient #6, a complete isolation case, and Patient #2, a partial isolation case).

**FIGURE 5** The Radiofrequency Application Sites for the Marshall Bundle Isolation



The **red and blue tags** indicate the radiofrequency application sites from the left atrium and coronary sinus, respectively. LAO = left anterior oblique; PA = posterior-anterior.

Among 4 patients who underwent RF applications only from the LA, 3 maintained SR during the follow-up and consisted of cases with a complete MB isolation, partial isolation, and failure case.

## DISCUSSION

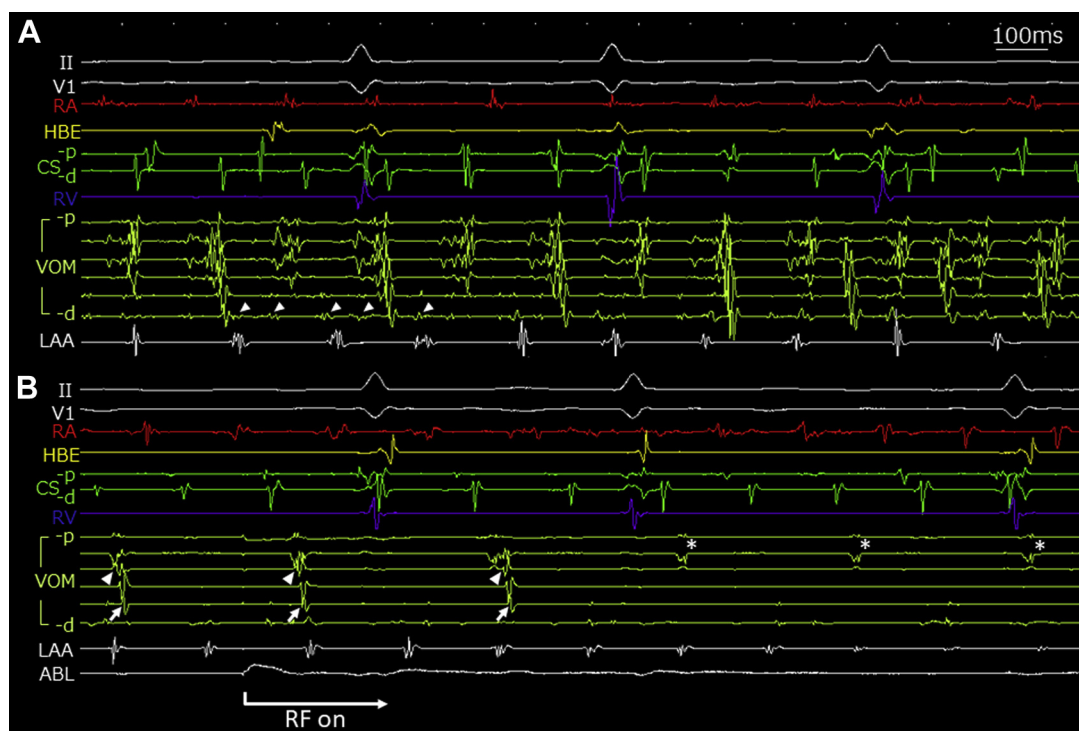
**MAJOR FINDINGS.** To the best of our knowledge, this is the first study to evaluate the RF intervention for the MB with a 2-F octapolar catheter inserted into the VOM. The complete isolation of the MB could be achieved in one-third of the patients with an arrhythmogenic MB and a partial isolation in another third of the patients, whereas the rest could not be isolated.

**PREVIOUS REPORTS.** The VOM was circumferentially surrounded by the MB close to the CS and diminished as it traveled more remotely from the CS (7). Furthermore, 1 or more electric connections existed between the MB and LA or CS (8). Notably, approximately 36% of the MBs had continuous extensive connections to the LA (7). In such cases, an

electric MB isolation would be difficult. Partial isolation of the VOM might suggest a conduction block of the midportion of the MB or isolation of the MB around the VOM, which existed in a partial manner and not circumferentially. Huang et al. (3) reported the cannulation of a quadripolar catheter into the VOM and terminated AF by eliminating the VOM electrograms using RF. Furthermore, they reported that a minority of the patients whose MB could not be ablated by RF from the endocardium due to a thick myocardium required epicardial mapping (9). In our study, 4 patients underwent endocardial ablation exclusively, and 2 of them experienced a partial isolation of the MB (i.e., distal isolation of the MB in 1 and unsuccessful isolation of the MB in the other, which might indicate that RF applications from both the LA and CS might be mandatory to achieve complete isolation of the MB even though complete MB isolation was obtained by an exclusively endocardial ablation). Another report showed the existence of an electric connection between the left superior PV and MB, which indicated that MB isolation should be



**FIGURE 6** Partial Isolation of the Marshall Bundle Potentials



**(A)** Arrhythmogenicity of the Marshall bundle during atrial fibrillation. The cycle lengths of the activation on the electrograms recorded by the electrodes in the vein of Marshall (**arrowheads**) during atrial fibrillation were shorter than those of the coronary sinus and left atrial appendage. **(B)** Partial isolation of the Marshall bundle. The Marshall bundle potentials recorded by the electrodes in the distal part of the vein of Marshall were eliminated by a radiofrequency application during atrial fibrillation (**arrows, arrowheads**). The **asterisks** indicate the residual proximal Marshall bundle potentials after the ablation. ABL = ablation catheter; other abbreviations as in [Figures 1 and 2](#).

**TABLE 2** Comparison of the Complete Isolation, Partial Isolation, and Failure Groups

	Complete Isolation (n = 7)	Partial Isolation (n = 7)	Failure (n = 6)	p Value
Age, yrs	69 (63-70)	70 (68-74)	57 (49-65)	NS
LA, mm	48 (41-50)	44 (39-46)	38 (35-41)	NS
Number of electrodes inserted into the VOM	7 (6-8)	7 (6-8)	7 (6-7)	NS
Voltage of the VOM electrogram before the RF application, mV	2.0 (0.9-2.6)	1.2 (0.8-1.8)	1.0 (0.7-1.2)	NS
Cumulative delivered energy to the VOM, J	10,460 (6,578-11,388)	9,655 (8,010-12,793)	21,233 (17,209-30,885)	<0.01
Number of RF applications for the VOM from the LA	10 (5-12)	10 (8-14)	17 (17-34)	<0.05
Number of RF applications for the VOM from the CS	5 (3-7)	3 (1-4)	7 (5-9)	NS
Duration of the RF applications for the VOM from the LA, s	159 (110-266)	246 (196-324)	527 (465-795)	<0.01
Duration of the RF applications for the VOM from the CS, s	113 (61-118)	37 (9-69)	126 (115-140)	NS
Total irradiation dose (mGy)	266 (222-382)	247 (189-296)	359 (203-724)	NS
Total fluoroscopy time (min)	37 (36-47)	42 (35-46)	52 (36-60)	NS
Total procedural time (min)	237 (222-243)	245 (200-275)	251 (219-366)	NS

Values are median (interquartile range).

CS = coronary sinus; LA = left atrium; NS = not significant; RF = radiofrequency; VOM = vein of Marshall.

considered after PV isolation (10) and RF application inside the left PV might be considered to achieve MB isolation in some cases.

Huang et al. (3) reported that the VOM could be visualized by balloon occlusion coronary sinus angiography in 19 of 28 patients (68%), and an electrode catheter could be inserted into the VOM in 17 patients (61%). Valderrabano et al. (2) reported that the VOM could be cannulated in 6 of 9 patients (67%). We attempted to cannulate the VOM using a 6-F multipurpose catheter by directly engaging the CS when inserted through an SL sheath from the right femoral vein. Using this method, the VOM could be visualized in 83 of 104 patients (80%), and a 2-F catheter could be inserted into the VOM in 74 patients (71%), which was considered to be safe, feasible, and not inferior to the balloon occlusive method (Figure 1).

**ETHANOL INJECTION INTO THE VOM.** An ethanol injection into the VOM is widely known as a safe and useful method to cure MB-originating AF. After the ethanol injection, voltage maps of the LA revealed a low-voltage area corresponding to the localization of the VOM (2), which is also associated with the denervation of the VOM (11). Although it requires another balloon catheter for coronary intervention, the region size created by ethanol injection is difficult to be predicted, and a cardiac tamponade can also happen (12), the ethanol injection could be considered as a next strategy when RF application failed to isolate the arrhythmogenic MB.

**CLINICAL IMPLICATIONS.** The MB has been reported to be an important substrate for re-entry after AF ablation due to the epicardial connections (13). Additionally, the MB contains abundant sympathetic and parasympathetic nerve fibers and ganglions (8) and can be the source of ectopies. Hence, RF ablation targeting the MB is expected to prevent atrial tachyarrhythmias. Moreover, the prolongation of the CLs of the electric activation of a surviving MB during AF was observed even in cases of a partial isolation. Given that, despite the small number of cases, intervention for the MB might modulate the arrhythmic substrate even in cases with a partial isolation.

The circuit of the perimitral flutter could involve the MB after PV isolation and LMI linear ablation. The 2-F electrode catheter in the VOM often helped to find the residual connections on the epicardial side. RF applications targeting the VOM electrodes have also been reported to create a mitral isthmus block in

difficult cases (14). The electric connections between the MB and LA myocardium could be localized close to the superolateral mitral isthmus line, and the LMI linear ablation could modulate these connections.

**STUDY LIMITATIONS.** The number of patients was small because of the single-center design of the study. Because the average follow-up term was <2 years, a long-term follow-up and the outcome should be evaluated. Balloon occlusive venography could reveal a VOM that was missed by CS venography with a multipurpose catheter. The PV isolation could have affected the electric connections between the MB and PV or LA myocardium. It was unclear whether the patients who had a failure of the MB isolation had a continuous and dense connection between the MB and LA or the failure of the MB isolation was only due to technical problems.

## CONCLUSIONS

A complete and partial MB isolation are achieved in 35% each using RF ablation, with a failure rate of 30%. The elimination of the MB potentials recorded by the catheter electrodes in the VOM could be a definite endpoint in patients with an arrhythmogenic MB.

## AUTHOR DISCLOSURES

Dr. Takatsuki has received honoraria from Daiichi-Sankyo; and has received honoraria and consulting fees from Medtronic Japan. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** An arrhythmogenic MB, 1 of the non-PV foci of AF, could be isolated electrically by an RF energy delivery from the LA and CS. This procedure might be feasible for a satisfactory outcome in AF ablation.

**TRANSLATIONAL OUTLOOK:** MB isolation was not exclusively performed; the type of intervention that led to a better outcome could not be confirmed. A randomized comparison test should be performed.

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**KEY WORDS** atrial fibrillation, isolation, Marshall bundle, radiofrequency ablation, vein of Marshall