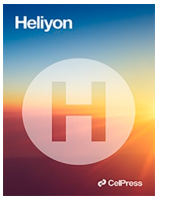
Heliyon 9 (2023) e21266

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Angiographic assessment of vein of Marshall in atrial fibrillation: Implications for identification and cannulation

Hong-Da Zhang [a,1], Lei Ding [a,1], Feng-Yuan Yu [a], Li-Jie Mi [a], Kuo Zhang [a], Si-Xian Weng [b], Zi-Han Jiang [a], Min Tang [a,*]

[a] *State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, 100037, China*

[b] *National Center for Clinical Laboratories, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing Hospital, National Center of Gerontology, Beijing, China*

ARTICLE INFO

Keywords:
Atrial fibrillation
The vein of Marshall
Ethanol infusion
Coronary vein angiography
Morphology assessment

ABSTRACT

Background: The vein of Marshall (VOM) ethanol infusion improves rhythm control in atrial fibrillation (AF). The identification and cannulation of the VOM can be technically challenging. This study aimed to assess the angiographic morphology of the VOM and investigate its value in the VOM ethanol infusion.

Methods: Patients with AF (n = 162) scheduled for combined catheter ablation and VOM ethanol infusion were enrolled. The VOM morphologic features in the right anterior oblique (RAO), the left anterior oblique (LAO), and the LAO cranial views were analyzed. The impact of morphology on the identification and cannulation of the VOM was investigated.

Results: The VOM was identified in 159 (98.1 %) and cannulated in 150 (92.6 %) patients. The VOM identification rate in the RAO and LAO/LAO cranial view was 97.3 % and 89.3 %, respectively. Of 134 patients with VOM identification in the LAO/LAO cranial view, 104 (77.6 %) had a VOM ostium clock location ($VOMo^{Clock}$) of ≤3 and 3–4 o'clock. The VOM cannulation success rate in the ≤3, 3–4, 4–5, and 5–6 o'clock groups was 100 %, 92.6 %, 88.5 %, and 77.8 %, respectively ($p = 0.032$). The median (interquartile range) cannulation time in the four groups was 10.5 (6.3), 12.0 (9.0), 13.0 (23.0), and 34.0 (30.0) minutes, respectively ($p < 0.001$). The diameter of the coronary sinus ostium in the RAO view and the $VOMo^{Clock}$ were independent predictors for difficult cannulation.

Conclusions: The VOM morphologic features in different angiographic views provide valuable information which could facilitate the identification and cannulation of the VOM.

1. Introduction

It was John Marshall who initially described the vein of Marshall (VOM) in 1850, describing it as a small oblique vein, the remnant of a primitive vessel running along the back of the left auricle [1]. He also described the ligament of Marshall (LOM) as the vestigial fold that comprises the VOM, some fibrous bands, and nervous filaments [1]. Contemporary pathological studies have shown that the

* Corresponding author. Fuwai Hospital, 167 Beilishi Road, Beijing, 100037, China.
E-mail address: doctortangmin@yeah.net (M. Tang).

[1] These authors contributed equally to this study.

https://doi.org/10.1016/j.heliyon.2023.e21266
Received 6 February 2023; Received in revised form 9 October 2023; Accepted 18 October 2023
Available online 20 October 2023

Abbreviations and acronyms

AF	atrial fibrillation
VOM	vein of Marshall
LOM	ligament of Marshall
RAO	the right anterior oblique
LAO	the left anterior oblique
VOMo	VOM ostium
CS	coronary sinus
CSo	CS ostium
$VOMo^{Clock}$	the VOMo clock-location
$VOMo^{Diameter}$	the diameter of the VOMo
$CSo^{Diameter}$	the diameter of the CS ostium
$CS@VOMo^{Diameter}$	the diameter of CS at the VOMo level
$VOMo\text{-}CSo^{Distance}$	the distance from VOMo to CSo
$VOMo\text{-}CSo^{Height}$	the vertical distance from VOMo to the roof of CSo
$VOM\text{-}CS^{Angle}$	the angle of VOM and CS
SD	standard deviation
IQR	interquartile range
ROC	receiver operative characteristic curve

LOM consists of various sympathetic nerve fibers, ganglia, blood vessels, and multiple myocardial tracts [2]. Over the past two decades, research has indicated that the VOM/LOM area is linked to atrial tachyarrhythmias, especially atrial fibrillation (AF) [3,4].

Several teams have been dedicated to performing VOM ethanol infusion in patients with AF [5–12]. The VENUS trial demonstrated that in patients with persistent AF, treatment with combined catheter ablation and VOM ethanol infusion had better outcomes compared with catheter ablation alone [6]. Another study showed that the success rate of the combined procedure in patients with persistent AF at 1 year was 79 %, which was promising [13].

For an electrophysiology lab of low volume to perform VOM ethanol infusion effectively, a deep understanding of the fluoroscopic anatomy and angioplasty tool is necessary, as this comes with a learning curve [4,7]. The first obstacle in the procedure is the identification of the VOM because the VOM lumen is extremely narrow, with the mean diameter of the VOM ostium (VOMo) lesser than 2 mm [12]. The cannulation of VOM can be tricky because the three-dimensional relationship between the VOM and coronary sinus (CS) seen under fluoroscopy might not be accurate. A study introduced an optimized computed tomography acquisition tool to visualize the VOM [14]. Nevertheless, analyzing the computed tomography images necessitates more time. Recently we have established a simple and feasible angiographic protocol to facilitate the identification of the VOM [12]. This study sought to comprehensively evaluate the angiographic features of the VOM in patients with AF using an updated protocol and investigate the impact of morphology on the identification and cannulation of the VOM.

2. Methods

2.1. Study population

Between November 2021 and September 2022, patients with AF who were scheduled for combined radiofrequency catheter ablation and ethanol infusion in Fuwai Hospital (Beijing, China) were consecutively enrolled. Candidates for the combined procedure were patients with persistent AF. Patients with paroxysmal AF who were in AF rhythm before the procedure and with low-voltage areas in the mitral isthmus were also enrolled. We performed voltage mapping in all patients before ablation using the three-dimensional mapping system (CARTO 3, Biosense Webster Inc., Diamond Bar, CA, USA). The definition of low voltage was a bipolar voltage of $<$0.5 mV. Patients in whom ethanol infusion failed were not included in further angiographic assessment (Fig. 1). This study was performed in accordance with the Declaration of Helsinki and was approved by the Review Board and Ethics Committee of Fuwai Hospital (Approval No. 2022-1810). Informed consent was obtained from all participants.

2.2. The combined procedure

Patients were sedated using midazolam and fentanyl in the electrophysiology lab, and then the antral pulmonary vein isolation was performed with or without additional linear ablation. After catheter ablation, coronary vein angiography was performed. Ethanol infusion of VOM was further performed if the VOM was identifiable and could be cannulated. After ethanol infusion, the mitral isthmus was ablated to achieve a bidirectional conduction block.

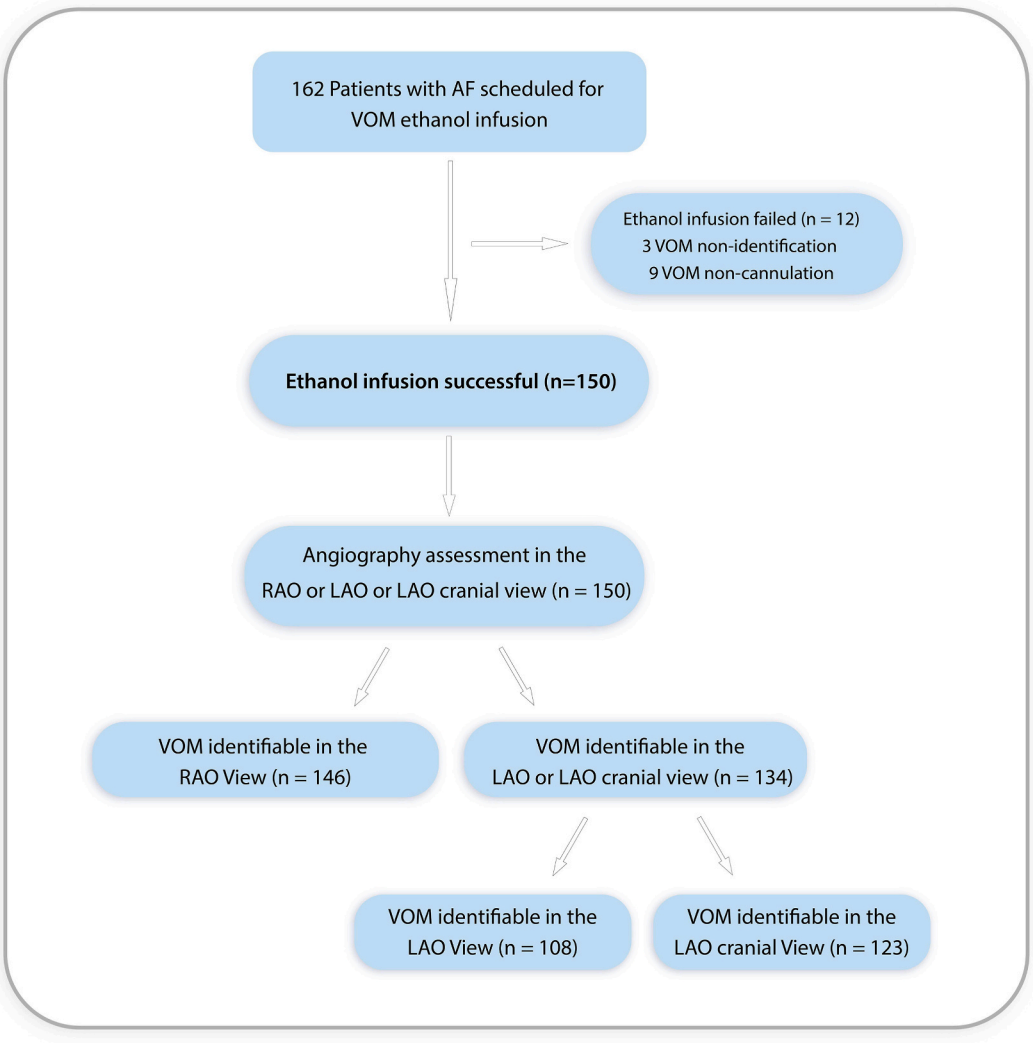


Fig. 1. Flow chart of patient enrollment AF, atrial fibrillation; VOM, the vein of Marshall; RAO, right anterior oblique; LAO, left anterior oblique.

2.3. VOM identification and cannulation

For coronary vein angiography, a guiding catheter (6-F Judkins Right [JR] 4; Medtronic, Minneapolis, MN, USA) was positioned inside the CS through an SL1 long sheath (8.5F; St. Jude Medical, Inc., St Paul, MN, USA) or a steerable long sheath (8.5-F, Agilis NxT; Abbott, St Paul, MN, USA) inserted from the right femoral vein. A stepwise angiography method has been reported by us recently [12]. We always began with the right anterior oblique (RAO) 30° view, followed by the left anterior oblique (LAO) 30° view, and then the LAO 30° cranial 20–30° view (Fig. 2). We did not perform coronary vein angiography in the anterior-posterior view. We performed non-occlusion angiography in three fluoroscopic views and at least three positions of the guiding catheter in the CS lumen from distal to proximal (maximum nine times angiography for identification of the VOM). The balloon occlusion angiography was not used. After identification of the VOM, an over-the-wire angioplasty balloon (1.5–2.5 mm diameter and 8–12 mm length; Boston Scientific, Cambridge, MA, USA) preloaded with an angioplasty wire was advanced into the guiding catheter and then positioned into the distal VOM. After successful cannulation, the balloon was inflated, and ethanol was delivered at 2–3 positions distally to proximally in the VOM. The cannulation time was defined as the time from the beginning of coronary vein angiography to the successful cannulation of the VOM. A cannulation time greater than 30 min was defined as difficult cannulation.

2.4. Angiography measurements

A comprehensive VOM morphology assessment consisted of the following parameters: 1) the VOMo clock-location ($VOMo^{Clock}$); 2) the diameter of the VOMo ($VOMo^{Diameter}$); 3) the diameter of CS at the VOMo level ($CS@VOMo^{Diameter}$); 4) the diameter of the CS ostium ($CSo^{Diameter}$); 5) the distance from VOMo to CSo ($VOMo\text{-}CSo^{Distance}$); 6) the vertical distance from VOMo to the roof of CSo

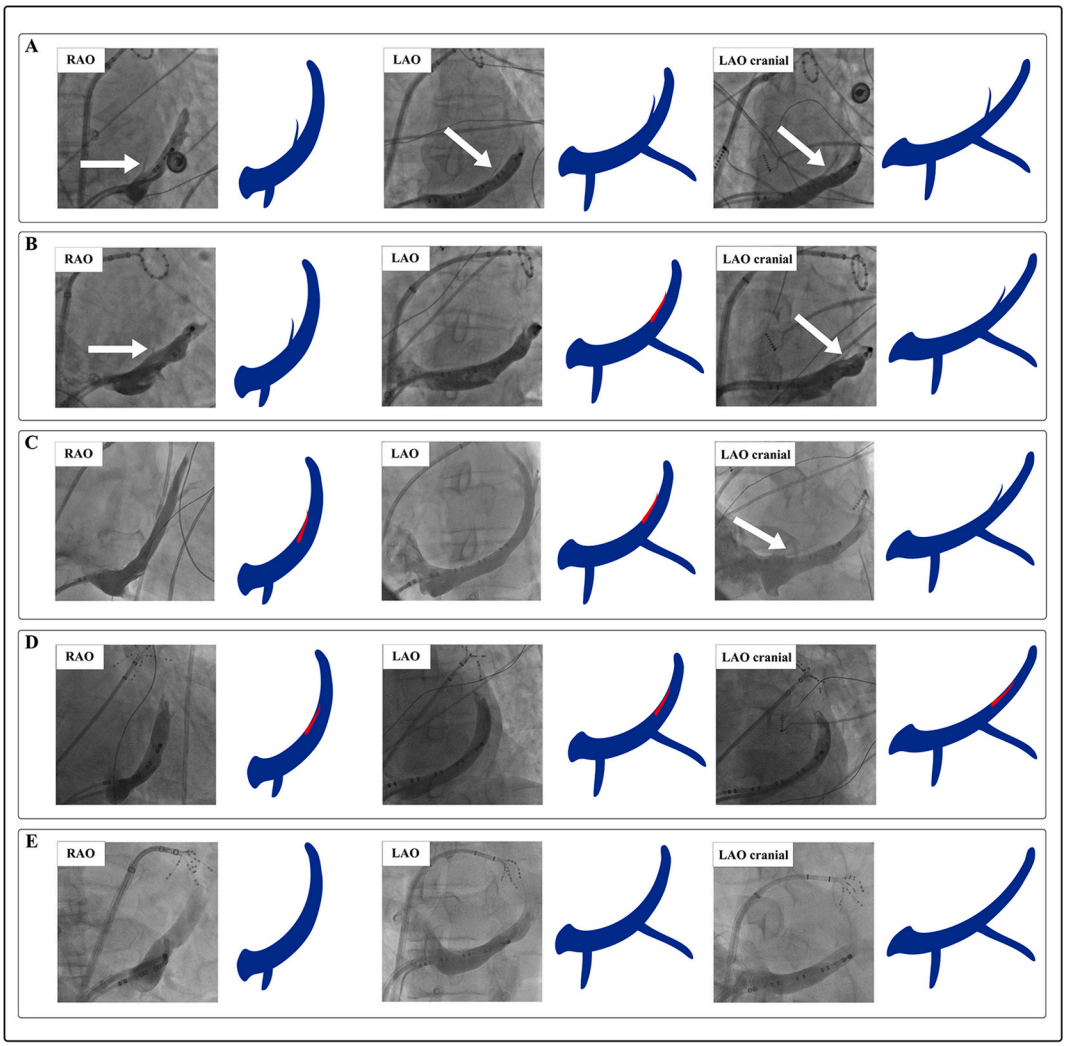
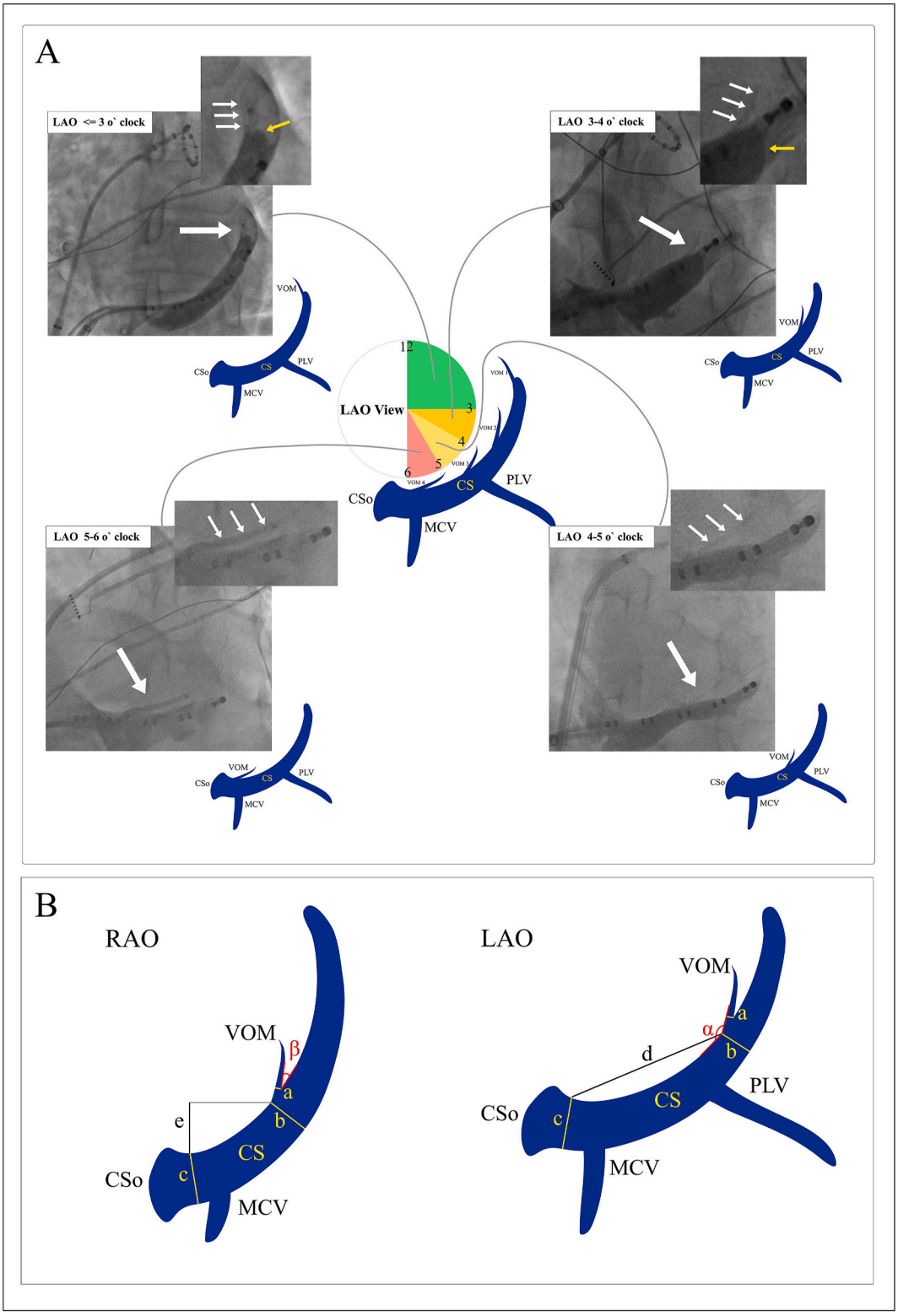


Fig. 2. The morphology of the VOM in different views A: The VOM could be identified in all three views; B: The VOM could be identified in the RAO and LAO cranial view but is barely seen in the LAO view; C: The VOM could only be identified in the LAO cranial view and is barely seen in the RAO and LAO view; D: The VOM probably exists but is barely seen in all three views; E: The VOM probably does not exist.
VOM, the vein of Marshall; RAO, right anterior oblique; LAO, left anterior oblique. The arrow indicates the VOM; The red VOM means the VOM probably exists but is barely seen. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(VOMo-CSo^{Height}); 7) the angle of VOM and CS (VOM-CS^{Angle}) (Fig. 3). The VOMo^{Clock} was defined as the VOMo location along the mitral annulus in the LAO view (LAO cranial view if VOM was not identifiable in the LAO view), which was classified into four groups: ≤3 o'clock, 3–4 o'clock, 4–5 o'clock, and 5–6 o'clock (Fig. 3A). The definitions of other parameters are shown in Fig. 3B; some have been reported by us recently [12]. All the parameters were measured independently by two authors using the Weasis software (Version 3.8.0).

2.5. Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]) as appropriate, and categorical variables are shown as ratio or percentage. For continuous data, the student t-test or Mann-Whiney *U* test was conducted between two independent samples as appropriate. For comparisons of continuous data among multiple groups, analysis of variance or non-parametric analyses were used when the assumption of normality was in doubt. The Chi-square test was used for the comparison of categorical data. The unadjusted associations between the clinical and angiographic parameters were assessed using Spearman rank correlation. Further association of cannulation time with clinical and angiographic parameters was analyzed in the logistic regression model. Demographic and clinical parameters, VOMo^{Clock} data, and angiography data in the RAO view were first analyzed in the univariate logistic regression model. Variables with a p-value <0.05 in the univariate logistic regression analysis were included in the



(caption on next page)

Fig. 3. The angiographic assessment of the VOM in different views. A: The locations of the VOM in the LAO view; B: Detailed measurement of the VOM.
VOM, the vein of Marshall; VOMo, VOM ostium; RAO, right anterior oblique; LAO, left anterior oblique; CS, coronary sinus; CSo, CS ostium; MCV, middle cardiac vein; PLV, posterior lateral vein; a, the diameter of VOMo; b, the CS diameter at the VOMo; c, the diameter of CSo; d, the distance from VOMo to CSo; e, the vertical distance of VOMo to the roof of CSo; α, the angle of VOM and CS in the LAO view; β, the angle of VOM and CS in the RAO view.
The white arrow indicates VOM; the yellow arrow indicates the valve of Vieussens.
The numbers in the pie chart indicate the VOMo clock location along the mitral annulus in the LAO view (LAO cranial view if VOM was not identifiable in the LAO view); VOM 1–4 represents the four hypothetical locations and does not mean four VOMs for one CS. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

multivariate-adjusted logistic regression model. A receiver operative characteristic curve (ROC) was used to determine the best cutoff values of predictors. A p-value of <0.05 was considered statistically significant. Data analyses were performed using R version 4.1.2.

3. Results

3.1. Patient characteristics and procedural parameters

A total of 162 patients were scheduled for the procedure (Fig. 1). Ethanol infusion failed in 12 patients, 3 for VOM non-identification and 9 for VOM non-cannulation. Of these 9 patients, 3 failed for having a very short VOM, 2 failed for having a $VOMo^{Clock}$ of 5–6 o'clock, and another 4 for our inadequate experience in the early stage of the VOM ethanol infusion project.

The final identification and cannulation success rates were 98.1 % (159/162) and 92.6 % (150/162), respectively. The cannulation success rate in patients with identified VOM was 94.3 % (150/159). Finally, 150 patients were enrolled for further angiographic assessment, and 130 had persistent AF (Table 1). The median (IQR) age was 59 (12) years old, and 66.7 % were male.

3.2. Image characteristics of the VOM in different views

For patients with successful cannulation (n = 150), the VOM was identified in the RAO, LAO, and LAO cranial view in 146 (97.3 %), 108 (72.0 %), and 123 (82.0 %) patients, respectively (Fig. 1). In the overall cohort (n = 162), the VOM was identified in the RAO, LAO,

Table 1
Patient characteristics.

Parameters	Overall Cohort (n = 150)
Male gender, n(%)	100 (66.7)
BMI, kg/m^2	26.2 ± 3.5
Paroxysmal AF, n (%)	20 (13.3)
Persistent AF, n (%)	130 (86.7)
Age, yrs	59.0 (12.0)
CHA_2DS_2-VASc score	2 (2)
HAS-BLED score	0 (1)
Comorbidities	
Hypertension, n(%)	79 (52.7)
Diabetes mellitus, n(%)	29 (19.3)
Coronary artery disease, n(%)	21 (14.0)
Previous myocradial infarction, n(%)	3 (2)
Prior PCI/CABG, n(%)	6 (4)
Congestive heart failure	31 (20.7)
Previous TIA or stroke, n(%)	11 (7.3)
Peripheral arterial disease, n(%)	9 (6)
Open heart surgery, n(%)	9 (6)
NYHA-FC III/IV, n(%)	5 (3.3)
Echocardiography parameters	
Left atria dimension (AP), mm	43 (6)
Left atrial volume, ml	75 ± 28
LVEDD, mm	49 (6)
Ejection fraction, %	61 (8)

AF, atrial fibrillation; BMI, body mass index; CHA_2DS_2-VASc: congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke, vascular disease, age 65–74 years, sex category (female); HAS-BLED: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly (>65 years of age), concomitant drugs/alcohol; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; TIA: transient ischemic attack; NYHA-FC, New York Heart Association functional class; AP, anteroposterior; LVEDD: left ventricular end-diastolic dimension.

and LAO cranial view in 155 (95.7 %), 113 (69.8 %), and 131 (80.9 %) patients. In 101 (62.3 %) patients, the VOM can be identified in all three views, as shown in Fig. 2A. In 27 (16.7 %) patients, the VOM was not evident in the LAO view but can be revealed in the RAO and the LAO cranial view (Fig. 2B). In 4 (2.5 %) patients, the VOM could only be identified in the LAO cranial view (Fig. 2C). In 3 (1.9 %) patients, the VOM was not evident (Fig. 2D) or absent (Fig. 2E) in all three views.

The VOM could be identified in 134 patients in the LAO or LAO cranial view (Fig. 1) who had a $VOMo^{Clock}$ as defined in Fig. 3A. Of these patients, 104 (77.6 %) had a $VOMo^{Clock}$ of ≤3 and 3–4 o'clock, and 30 (22.4 %) had a $VOMo^{Clock}$ of 4–5 and 5–6 o'clock (Fig. 4A). Patients had a median (IQR) $VOMo^{Diameter}$ of 1.9 (1.1), 1.7 (0.8), and 1.8 (1.2) mm in the RAO, LAO, and LAO cranial view, respectively (Table 2). The median (IQR) $CSo^{Diameter}$ was 13.8 (5.7), 14.2 (6.6), and 15.1 (5.5) mm in the RAO, LAO, and LAO cranial view, respectively (Table 2).

3.3. Association between VOM morphology and cannulation time

Of all 159 patients with identified VOM, the VOM cannulation success rate in the ≤3, 3–4, 4–5, and 5–6 o'clock groups was 100 %, 92.6 %, 88.5 %, and 77.8 %, respectively (p = 0.032, Fig. 4B). Of all 150 patients with successful cannulation, the median (IQR) cannulation time was 12.0 (9.25) minutes. The median (IQR) cannulation time in the ≤3, 3–4, 4–5, and 5–6 o'clock groups was 10.5 (6.25), 12.0 (9.0), 13.0 (23.0), and 34.0 (30.0) minutes, respectively (p < 0.001, Fig. 4C). The median (IQR) cannulation time in the ≤4 and 4–6 o'clock groups was 11.0 (7.0) and 19.0 (25.5) minutes, respectively (p = 0.002, Fig. 4D).

There were weak but statically significant associations between cannulation time and the $VOMo\text{-}CSo^{Distance}$ in the RAO view, $CSo^{Diameter}$ in the RAO view, $CS@VOMo^{Diameter}$ in the RAO, $VOM\text{-}CS^{Angle}$ in the RAO view, $VOMo\text{-}CSo^{Distance}$ in the LAO view, and $VOMo\text{-}CSo^{Distance}$ in the LAO cranial view (Supplemental Fig. 1).

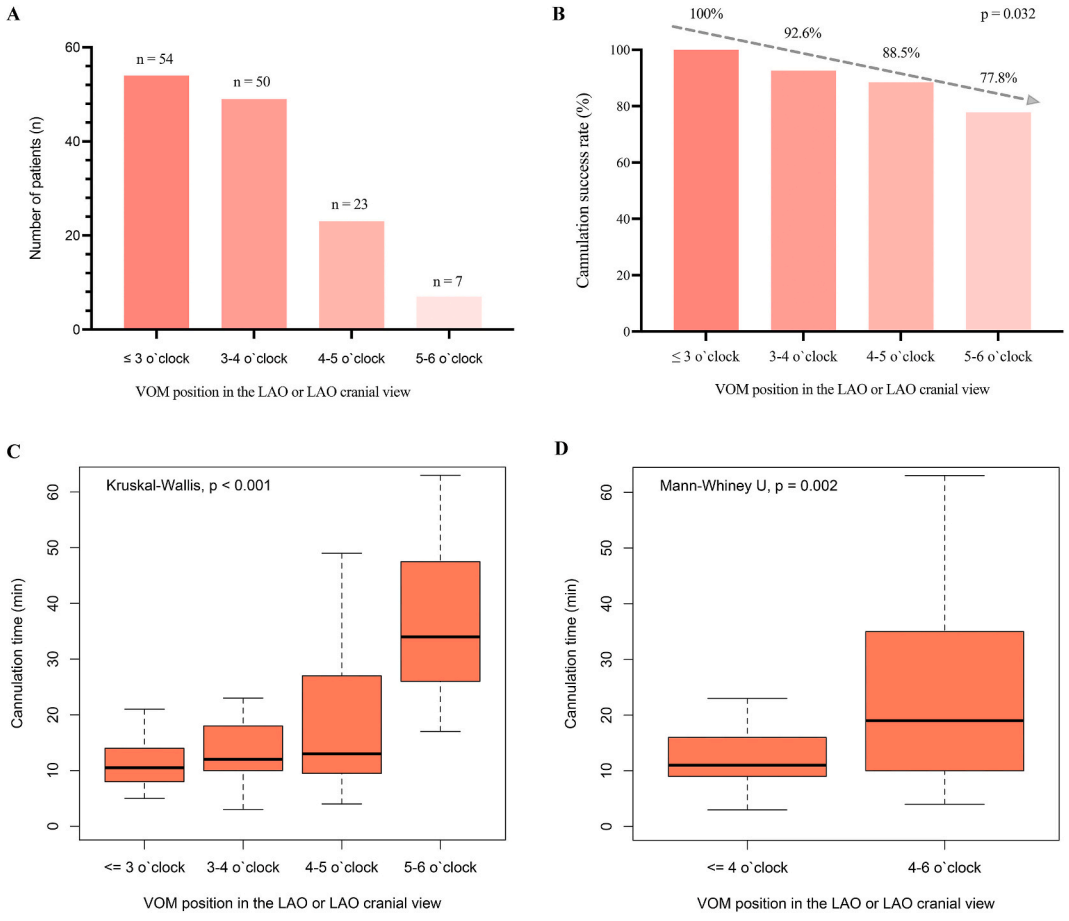


Fig. 4. The angiographic features in the LAO or LAO cranial view. A: The number of patients in different groups according to the VOM location; B: The cannulation success rates of patients in different groups according to the VOM location; C and D: The cannulation time of patients in different groups according to the VOM location.
VOM, the vein of Marshall; LAO, left anterior oblique.

Table 2
Angiography results.

Parameters	
RAO view available (n = 146)	
VOMo diameter, mm	1.9 (1.1)
CS diameter at VOMo, mm	9.9 (4.1)
CSo diameter, mm	13.8 (5.7)
Vertical distance from VOMo to CSo, mm	18.1 (18.5)
VOM-CS angle, degree	37.6 (25.0)
LAO view available (n = 108)	
VOMo diameter, mm	1.7 (0.8)
CS diameter at VOMo, mm	7.9 (3.5)
CSo diameter, mm	14.2 (6.6)
Distance from VOMo to Cso, mm	41.6 (17.5)
VOM-CS angle, degree	156.3 (15.7)
LAO cranial view available (n = 123)	
VOMo diameter, mm	1.8 (1.2)
CS diameter at VOMo, mm	8.8 (4.5)
CSo diameter, mm	15.1 (5.5)
Distance from VOMo to Cso, mm	44.3 (23.0)
VOM-CS angle, degree	150.7 (14.8)

RAO, right anterior oblique; LAO, left anterior oblique; VOM, vein of Marshall; VOMo, VOM ostium; CS, coronary sinus; CSo, CS ostium.

3.4. Predictors of difficult cannulation

In the overall cohort, 18 patients had difficult cannulation. Of the 134 patients with $VOMo^{Clock}$ and RAO view data, 16 had difficult cannulation. Finally, $VOMo^{Clock}$ and $CSo^{Diameter}$ in the RAO view were independent predictors of difficult cannulation (Table 3).

Correlations between difficult cannulation and $VOMo^{Clock}$ and $CSo^{Diameter}$ in the RAO view were further evaluated by ROC curves. The results showed that a smaller $CSo^{Diameter}$ in the RAO view (c-statistic = 0.7275, p = 0.002) and a greater $VOMo^{Clock}$ (c-statistic = 0.7994, $p < 0.001$) were associated with difficult annulation (Fig. 5A and B).

4. Discussion

This study provides a comprehensive assessment of the morphologic characteristics of the VOM in different fluoroscopic views. The results suggested that the RAO view could reveal the VOM in the majority of patients and that the LAO and LAO cranial view added additional value to the identification of the VOM. It was also demonstrated that the VOM location, as shown in the LAO/LAO cranial view, was related to the cannulation rate and could predict difficult cannulation of the VOM.

Table 3
Univariate and multivariate Logistic regression analysis of risk factors for difficult VOM cannulation.

	Unadjusted Odds Ratio (95 % CI)	p value	Adjusted Odds Ratio (95 % CI)	p value
$VOMo^{Clock}$		0.002		0.037
Reference (5–6 o'clock)				
4–5 o'clock	0.265 (0.045, 1.543)	0.139	0.194 (0.022, 1.724)	0.141
3–4 o'clock	0.085 (0.015, 0.495)	0.006	0.089 (0.009, 0.844)	0.035
< = 3 o'clock	0.014 (0.001, 0.169)	0.001	0.017 (0.001, 0.294)	0.005
Parameters in the RAO view				
VOMo diameter, mm	1.133 (0.858, 1.496)	0.380		
CS diameter at VOMo, mm	0.999 (0.857, 1.164)	0.990		
CSo diameter, mm	0.778 (0.652, 0.927)	0.005	0.782 (0.624, 0.980)	0.032
Vertical distance from VOMo to Cso, mm	0.961 (0.917, 1.006)	0.089		
VOM-CS angle, degree	1.032 (1.008, 1.057)	0.009	1.006 (0.977, 1.037)	0.673
Echocardiography parameters				
Left atria dimension (AP), mm	0.914 (0.816, 1.023)	0.118		
Left atrial volume, ml	0.982 (0.958, 1.006)	0.146		
LVEDD, mm	1.020 (0.935, 1.113)	0.658		
Ejection fraction, %	0.974 (0.922, 1.029)	0.344		
Demographics				
Age, years	0.943 (0.899, 0.989)	0.016	0.978 (0.925, 1.035)	0.443
Sex, female to male	0.759 (0.275, 2.095)	0.595		
BMI, kg/m^2	1.126 (0.983, 1.289)	0.086		

RAO, right anterior oblique; LAO, left anterior oblique; VOM, vein of Marshall; VOMo, VOM ostium; $VOMo^{Clock}$, VOMo location along the mitral annulus in the LAO view (LAO cranial view if VOM was not identifiable in the LAO view); CS, coronary sinus; CSo, CS ostium; BMI, body mass index; AP, anteroposterior; LVEDD: left ventricular end-diastolic dimension; CI, confidential interval.

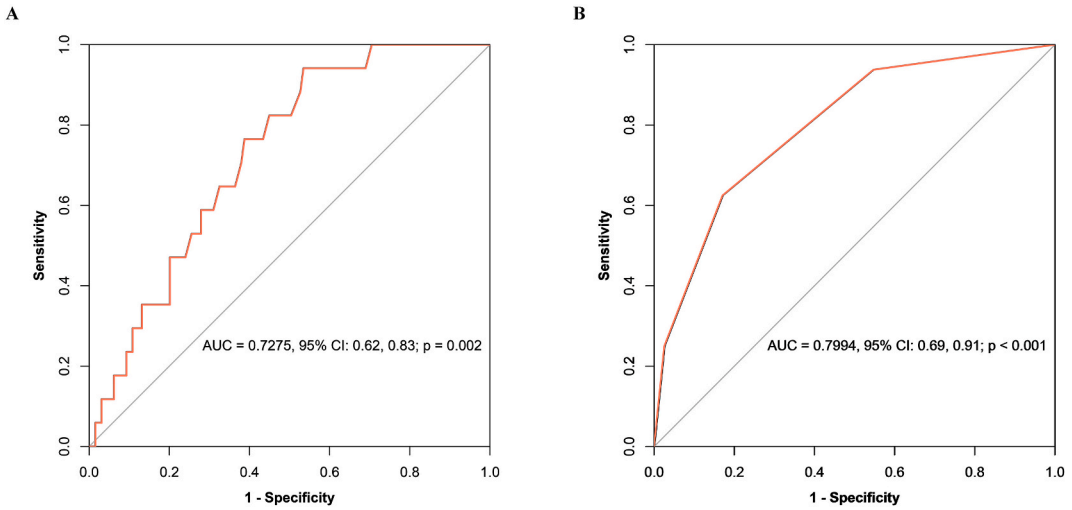


Fig. 5. ROC curves of predicting difficult cannulation. A: The predicting value of CSo diameter in the RAO view; B: The predicting value of $VOMo^{Clock}$.

ROC, receiver operative characteristic curve; AUC, area under curve; CI, confidential interval; VOM, the vein of Marshall; CSo, coronary sinus ostium; VOMo, VOM ostium; $VOMo^{Clock}$, VOMo location along the mitral annulus in the LAO view (LAO cranial view if VOM was not identifiable in the LAO view).

The French group reported a yearly increased success rate from 84.3 % in the first year to 92.6 % in the third year [7]. In the VENUS trial, the cannulation success rate was 83.7 % [6]. We started the VOM ethanol infusion project one year before the analysis. An identification rate of 98.1 % and cannulation success rate of 92.6 % in the first year is satisfactory and should be attributed to the detailed methods provided by previous studies [4,6,7,15]. Now, we have modified our protocol to increase the identification rate, as shown in Supplemental Fig. 2. The key is to find the VOM in three fluoroscopic views and at least three positions of the guiding catheter in the CS lumen from distal to proximal. However, this method might require more contrast media and radiation exposure than occluded angiography. Further studies are warranted to compare these two methods of angiography in terms of procedural time, amount of contrast media, and radiation exposure.

The RAO view, which is frequently employed, permits easy identification and differentiation of the VOM from other veins [4,6,7,15]. The LAO view, however, is underused for VOM ethanol infusion. We find the LAO view useful mainly in two scenarios, when the VOM is absent in the RAO view or when the cannulation is difficult in the RAO view. The first scenario is not commonly seen and only occurred in 4 (2.5 %) patients in this study. The VOM was finally identified in the LAO cranial view in these 4 patients, as shown in Fig. 2C. The second scenario is more frequently seen in our lab. In some patients, especially those with a $VOMo^{Clock}$ of $\leq$4 o'clock, the VOMo is distal to the CSo. The guiding catheter would be advanced distally in the CS lumen, in which case the whole picture of the guiding catheter may not be visible in the RAO view because of image overlapping. However, it is more clearly seen in the LAO or LAO cranial view, which makes it more convenient for manipulating guiding catheters (Supplemental Fig. 2). To conclude, the RAO view is the cornerstone for VOM ethanol infusion. Nevertheless, the LAO and the LAO cranial views can be utilized as alternatives to help identify and cannulate the VOM in challenging cases.

This is the first study to introduce the idea of $VOMo^{Clock}$, which was defined as the clock location of the VOMo in the LAO or LAO cranial view (Fig. 3A). It is extremely useful and has been routinely used in our lab for over one year. The VOMo varies in distance to the CSo, and this variability in distance may be more evident and easier to assess in the LAO or LAO cranial view. We could easily classify the VOMo locations into four groups during the procedures, from $\leq$3 to 5–6 o'clock (Fig. 3A). This facilitates communication with colleagues. More importantly, the $VOMo^{Clock}$ is related to the success rate of cannulation. In this study, most patients had a $VOMo^{Clock}$ of $\leq$3 and 3–4 o'clock, and the cannulation success rate was 100 % and 92.6 %, respectively (Fig. 4A and B). Only nine patients had a $VOMo^{Clock}$ of 5–6 o'clock, with a significantly lower cannulation success rate of 77.8 % compared to other groups (Fig. 4A and B).

The cannulation time ranged from 3 to 63 min in patients with successful cannulation. As shown in Fig. 4C and D, the cannulation time increased significantly from $VOMo^{Clock}$ of $\leq$3 to 5–6 o'clock. The schematic diagrams in Supplemental Fig. 2 can partially explain its reason. In Supplemental fig. 2C, which represents the $VOMo^{Clock}$ of 5–6 o'clock, the guiding catheter is positioned very proximally to the CSo, and it may slip off the CS lumen, even with the assistance of a steerable long sheath. A cannulation time of over 30 min is defined as difficult cannulation in our lab. When analyzed in a logistic regression model, the $VOMo^{Clock}$ was demonstrated to be an independent predictor for difficult cannulation. This was also verified in the ROC curve analysis. The result is consistent with our clinical experience that if a patient has $VOMo^{Clock}$ of $\leq$3 o'clock, the cannulation will be easy. The cannulation will take longer if a patient has a VOMoClock of 5–6 o'clock. In cases of $VOMo^{Clock}$ of 5–6 o'clock, using a special-sized or preformed guiding catheter or operating via the internal jugular might be a solution.

We obtained a set of parameters through various fluoroscopic views (Fig. 3B and Table 2). The $VOM\text{-}CS^{Angle}$ seemed smaller in the

LAO cranial view than in the LAO view (Table 2), which could explain that in some patients, the VOM was absent in the LAO view but present in the LAO cranial view (Fig. 2). The mean VOM-CS^{Angle} was 170.3 (ranging from 161.2 to 178.0) in the LAO cranial view in those four patients in whom the VOM could only be identified in this view. The diameter of VOMo was lesser than 2 mm in different views. However, it was not related to cannulation time (Table 3). This is technically true in our clinical experience because as long as the location of VOM is good, the cannulation would be easy, and the diameter of VOMo does not matter. The diameter of CSo in the RAO view had a statistically significant negative linear relationship with cannulation time and was also an independent predictor for difficult cannulation (Table 3, Fig. 5, and Supplemental Fig. 1). This is consistent with our clinical experience because a bigger CS gives us more space to operate the sheath and catheter. When the CS ostium is smaller in size, it can pose challenges in stabilizing the guiding catheter and increase the risk of over-rotation, leading to repeated misses of the ostium of the VOM. It is interesting that CS@VOMo^{Diameter} did not predict difficult cannulation. To gain a better understanding of this result, studies with larger sample sizes in the future may be necessary.

We always perform a CS angiography rather than a sub-selective VOM angiography. Because a sub-selective VOM angiography might cause dissection. The VOM dissection occurred in 4 (2.5 %) patients in this study, all because of accidently sub-selective VOM angiography. No patients in this study had pericardial effusion because of VOM ethanol infusion.

5. Limitations

Firstly, this was a retrospective analysis conducted in a single center with over 150 VOM ethanol infusions per year. Multicenter prospective studies are needed. Secondly, this was our first-year experience, and we believe the challenging cases will be solved in the future. Thirdly, we performed all the VOM ethanol infusions via the femoral vein with a high success rate. We might need to try the internal jugular vein in some challenging cases.

6. Conclusions

This study offers new insights into the angiographic characteristics of the VOM. It suggests that the LAO and LAO cranial views provide additional value in identifying the VOM compared to the conventional RAO view. The VOM location in the LAO or LAO cranial view is related to the cannulation success rate and could predict difficult cannulation of the VOM.

Ethics statement

This study was performed in accordance with the Declaration of Helsinki and was approved by the Review Board and Ethics Committee of Fuwai Hospital (Approval No. 2022-1810).

Funding

The study was supported by the National Natural Science Foundation of China (U1913210 and 82000064), and CAMS Innovation Fund for Medical Sciences (2022-I2M-C&T-B-047). The funding source had no role in study design; in the collection, analysis, and interpretation of data; in writing the report; and in the decision to submit the article for publication.

Data availability statement

Research data is confidential. Data-sharing requests are required to meet the policies of the hospital and the funder.

CRediT authorship contribution statement

Hong-Da Zhang: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Lei Ding:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Feng-Yuan Yu:** Data curation, Investigation, Methodology, Writing – review & editing. **Li-Jie Mi:** Investigation, Methodology, Writing – review & editing, Data curation. **Kuo Zhang:** Data curation, Investigation, Methodology, Writing – review & editing. **Si-Xian Weng:** Data curation, Investigation, Methodology, Writing – review & editing. **Zi-Han Jiang:** Data curation, Investigation, Methodology, Writing – review & editing. **Min Tang:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21266.

References

[1] J. Marshall, On the development of the great anterior veins in man and mammalia; including an account of certain remnants of fætal structure found in the adult, a comparative view of these great veins the different mammalia, and an analysis of their occasional peculiarities in the human subject, Phil. Trans. Roy. Soc. Lond. 140 (1850) 133–170.

[2] D.T. Kim, A.C. Lai, C. Hwang, L.T. Fan, H.S. Karagueuzian, P.S. Chen, M.C. Fishbein, The ligament of Marshall: a structural analysis in human hearts with implications for atrial arrhythmias, J. Am. Coll. Cardiol. 36 (2000) 1324–1327.

[3] R.N. Doshi, T.J. Wu, M. Yashima, Y.H. Kim, J.J. Ong, J.M. Cao, C. Hwang, P. Yashar, M.C. Fishbein, H.S. Karagueuzian, P.S. Chen, Relation between ligament of Marshall and adrenergic atrial tachyarrhythmia, Circulation 100 (1999) 876–883.

[4] M. Valderrábano, Vein of Marshall ethanol infusion in the treatment of atrial fibrillation: from concept to clinical practice, Heart Rhythm 18 (2021) 1074–1082.

[5] M. Valderrábano, X. Liu, C. Sasaridis, J. Sidhu, S. Little, D.S. Khoury, Ethanol infusion in the vein of Marshall: adjunctive effects during ablation of atrial fibrillation, Heart Rhythm 6 (2009) 1552–1558.

[6] M. Valderrábano, L.E. Peterson, V. Swarup, P.A. Schurmann, A. Makkar, R.N. Doshi, D. DeLurgio, C.A. Athill, K.A. Ellenbogen, A. Natale, J. Koneru, A.S. Dave, I. Giorgberidze, H. Afshar, M.L. Guthrie, R. Bunge, C.A. Morillo, N.S. Kleiman, Effect of catheter ablation with vein of Marshall ethanol infusion vs catheter ablation alone on persistent atrial fibrillation: the VENUS randomized clinical trial, JAMA 324 (2020) 1620–1628.

[7] T. Kamakura, N. Derval, J. Duchateau, A. Denis, T. Nakashima, T. Takagi, F.D. Ramirez, C. André, P. Krisai, Y. Nakatani, R. Tixier, R. Chauvel, G. Cheniti, K. Kusano, H. Cochet, F. Sacher, M. Hocini, P. Jaïs, M. Haïssaguerre, T. Pambrun, Vein of Marshall ethanol infusion: feasibility, pitfalls, and complications in over 700 patients, Circ Arrhythm Electrophysiol 14 (2021), e010001.

[8] Y. Lai, X. Liu, C. Sang, D. Long, M. Li, W. Ge, X. Liu, Z. Lu, Q. Guo, C. Jiang, S. Zuo, C. Jiang, R. Bai, R. Tang, X. Guo, S. Li, N. Liu, W. Wang, X. Zhao, C. Li, X. Du, J. Dong, C. Ma, Effectiveness of ethanol infusion into the vein of Marshall combined with a fixed anatomical ablation strategy (the "upgraded 2C3L" approach) for catheter ablation of persistent atrial fibrillation, J. Cardiovasc. Electrophysiol. 32 (2021) 1849–1856.

[9] C.M. Liu, L.W. Lo, Y.J. Lin, C.Y. Lin, S.L. Chang, F.P. Chung, T.F. Chao, Y.F. Hu, T.C. Tuan, J.N. Liao, Y.Y. Chen, L. Kuo, T.Y. Chang, Q.M. Hoang, S. Salim, J.J. B. Vicera, C.I. Wu, C.M. Chuang, T.C. Huang, S.A. Chen, Long-term efficacy and safety of adjunctive ethanol infusion into the vein of Marshall during catheter ablation for nonparoxysmal atrial fibrillation, J. Cardiovasc. Electrophysiol. 30 (2019) 1215–1228.

[10] C. Sang, Y. Lai, D. Long, M. Li, R. Bai, C. Jiang, W. Wang, S. Li, R. Tang, X. Guo, N. Liu, X. Zhao, S. Zuo, S. Wen, M. Ning, J. Wu, X. Du, J. Dong, C. Ma, Ethanol infusion into the vein of Marshall for recurrent perimitral atrial tachycardia after catheter ablation for persistent atrial fibrillation, Pacing Clin. Electrophysiol. 44 (2021) 773–781.

[11] M. Laredo, V. Ferchaud, O. Thomas, G. Moubarak, B. Cauchemez, A. Zhao, Durability of left atrial lesions after ethanol infusion in the vein of Marshall, JACC Clin. Electrophysiolog. 8 (2021) 41–48.

[12] L. Ding, H. Zhang, F. Yu, L. Mi, W. Hua, S. Zhang, Y. Yao, M. Tang, Angiographic characteristics of the vein of Marshall in patients with and without atrial fibrillation, J. Clin. Med. (2022) 11.

[13] N. Derval, J. Duchateau, A. Denis, F.D. Ramirez, S. Mahida, C. André, P. Krisai, Y. Nakatani, T. Kitamura, M. Takigawa, R. Chauvel, R. Tixier, X. Pillois, F. Sacher, M. Hocini, M. Haïssaguerre, P. Jaïs, T. Pambrun, Marshall bundle elimination, Pulmonary vein isolation, and Line completion for ANatomical ablation of persistent atrial fibrillation (Marshall-PLAN): prospective, single-center study, Heart Rhythm 18 (2021) 529–537.

[14] T. Takagi, N. Derval, T. Pambrun, Y. Nakatani, C. Andre, F.D. Ramirez, T. Nakashima, P. Krisai, T. Kamakura, X. Pineau, R. Tixier, R. Chauvel, G. Cheniti, J. Duchateau, F. Sacher, M. Hocini, M. Haissaguerre, P. Jais, H. Cochet, Optimized computed tomography acquisition protocol for ethanol infusion into the vein of Marshall, JACC Clinical electrophysiology 8 (2022) 168–178.

[15] P. Krisai, T. Pambrun, Y. Nakatani, T. Nakashima, T. Takagi, T. Kamakura, C. André, G. Cheniti, R. Tixier, R. Chauvel, J. Duchateau, F. Sacher, M. Haïssaguerre, H. Cochet, P. Jaïs, N. Derval, M. Hocini, How to perform ethanol ablation of the vein of Marshall for treatment of atrial fibrillation, Heart Rhythm 18 (2021) 1083–1087.