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Transplant & Mechanical Support: Mini Review

The Ligament of Marshall: Far From Vestigial!

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ABSTRACT

BACKGROUND The ligament of Marshall (LOM) is a vestigial fold of the left atrium that contains the remnant left cardinal vein, muscle bundles, and nerve fibers. Despite its description as an embryologic remnant, the LOM carries significant clinical importance as an important focus for atrial fibrillation propagation as well as a therapeutic target.

METHODS In this review, we discuss the embryologic origins of the LOM, its physiology and importance in atrial fibrillation pathogenesis, as well as the role of targeting and ablating the LOM surgically during concomitant cardiac surgery including lung transplantation.

RESULTS The LOM, particularly its distal segment, is an important focus for atrial fibrillation as both a primary trigger as well as an accessory bundle for signal propagation. It is a key target for electrophysiologic therapies including radiofrequency and alcohol-based ablative strategies. The LOM is also a crucial target for surgical ablation while addressing the left atrial lesion sets. This is often performed concomitantly with other cardiac surgical operations and may play an important role in reducing the risk of postoperative atrial fibrillation after lung transplantation.

CONCLUSIONS Far from just a vestigial structure, the ligament of Marshall remains an important focus for paroxysmal atrial fibrillation and is a potent therapeutic target for both electrophysiologic and surgical approaches.

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IN SHORT

- The ligament of Marshall (LOM) is a vestigial fold of the left atrium that is an important focus for atrial fibrillation (AF).
- The LOM is a key therapeutic target for both electrophysiologic and surgical ablation.
- LOM ablation during lung transplantation may be important in reducing the risk of postoperative AF.

The ligament of Marshall (LOM) is a vestigial left atrial fold that is classically found between the left superior pulmonary vein (PV) and the pulmonary artery. This structure contains the left cardinal vein, nerve fibers, small vessels, muscle bundles (termed "Marshall bundles") and the embryonic situs venosus.[1,2] This curious structure carries substantial clinical significance, particularly with respect to atrial fibrillation (AF), as one of the primary foci for paroxysmal AF and persistent AF. As such, it is a potent potential therapeutic target not only for electrophysiologic ablation, but also surgical ablation.[2]

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Abbreviations and Acronyms

AF = atrial fibrillation
CA = catheter-based ablation
LOM = ligament of Marshall
LPV = left pulmonary vein
PV = pulmonary vein
PVI = pulmonary vein isolations
RFA = radiofrequency ablation
SA = surgical ablation

MATERIAL AND METHODS

In this review, we highlight the clinicopathologic significance of the LOM, reflect on the efficacy of ablation of the LOM on reducing the risk of postoperative AF, and discuss the technical considerations of surgical LOM ablation during concomitant cardiothoracic operations including lung transplantation.

RESULTS

EMBRYOLOGIC ORIGINS OF THE LOM. The LOM is the vestigial remnant of visceral pericardium that contains the left common cardinal vein, muscle fibers, and nerves.[3,4] It was historically described as a remnant structure of the embryonic left superior vena cava by British surgeon John Marshall.[5] During embryogenesis, the anterior cardinal vein connects with the subclavian vein and Cuvier duct (which develops into the coronary sinus). The anterior cardinal vein empties into a primitive sinoatrial chamber and the left cardinal vein then involutes, leaving behind the vein of Marshall.[6]

ANATOMIC PRINCIPLES AND PHYSIOLOGY. The LOM is activated from the coronary sinus and the signal is propagated down the atrial free wall. It is anatomically divided into the proximal, middle, and distal segments.[7] The proximal LOM is connected to the coronary sinus; the middle LOM connects the left PV (LPV) to the left lateral ridge while the distal segment extends past the LPV (Figure).[7] The distal LOM is most commonly implicated in AF generation.[8] Histologically, the nerve fibers in the LOM contain both sympathetic and parasympathetic fibers. The epicardial muscle fibers in the LOM are often implicated in reentrant circuits.[9] Physiologically, the LOM participates in conduction over the lateral mitral isthmus and to the left-sided pulmonary vein and connects the coronary sinus, pulmonary veins, and the left lateral ridge.[10] The LOM, therefore, is both an important primary trigger and accessory bundle for propagation of AF, as part of the left atrial reentrant circuit.[1]

THE LOM AS THERAPEUTIC TARGET FOR AF. Electrophysiologically, the LOM is a promising target for catheter-based ablation, though only approximately 22% of electrophysiology labs specifically survey the LOM during AF ablation sessions, which often consist of empiric pulmonary vein isolations (PVI) using either radiofrequency ablation (RFA) or cryoablation.[7,11] Addition of other lesion sets, particularly superior vena cava isolation, may enhance ablation efficacy.[12] When targeting the LOM, endocardial mapping is typically performed using a coronary sinus catheter through which a venogram is performed to identify the vein of Marshall, which is then cannulated for mapping. Epicardial mapping can also be performed.[7] Once targeted, the LOM can be ablated with RFA or alcohol-based chemical ablation. In a series of 28 patients with paroxysmal atrial fibrillation, 6 patients had AF originating from the LOM, and RFA terminated AF in 4 of these patients.[13] Furthermore, selective targeting and RFA of the LOM after failed AF ablation through pulmonary vein isolation or mitral isthmus block may provide increased clinical benefit.[14] Catheter ablation alone, however, has had mixed results; simultaneous ethanol infusion and RFA ablation has been associated with greater long-term freedom from AF and atrial tachycardia.[15] A possible reason for the mixed efficacy of LOM targeting may be that the lesion may be difficult to accurately localize; unipolar electrograms may be superior to bipolar electrograms in this regard.[10]

THE LOM AS A TARGET FOR SURGICAL ABLATION. Despite these strategies, the long-term efficacy of catheter-based ablation (CA) compared to surgical ablation is controversial. Indeed, in the setting of standalone AF, a randomized trial investigating first-line minimally invasive thoracoscopic pulmonary vein ligation + left atrial appendage ligation v. CA for primary AF treatment demonstrated that CA was noninferior to surgical ablation (SA), with respect to arrhythmia-free survival at 2 years.[16] However, it is important to note that CA (which primarily isolates the pulmonary veins) has demonstrated mixed long-term efficacy, particularly with larger left atrial diameter and right atrial non-PV ectopy.[17,18] To this point, The Atrial Fibrillation Catheter Ablation vs. Surgical Ablation Treatment (FAST) trial of 124 patients with drug-refractory AF with dilated left atrium and hypertension or those with failed prior CA found

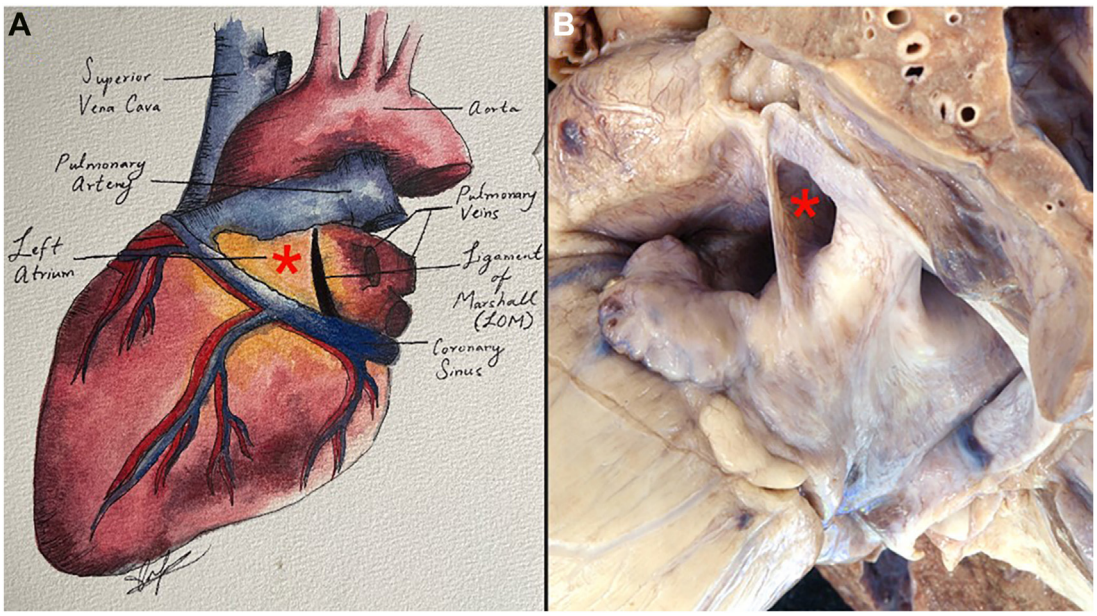

FIGURE (A) Pictographic depiction and (B) cadaveric photograph of the ligament of Marshall (*) arising from the coronary sinus between the left atrial appendage and left pulmonary veins. Panel B used with permission from Dr Diane Spicer. Figure constructed on Biorender.com.

that those patients randomized to SA compared to CA demonstrated that freedom from left atrial arrythmia >30 seconds without pharmacotherapy at 12 months was 65.6% vs 36.5%, respectively ($P = .0022$).[17] As with catheter-based AF ablation, targeting and ablating the LOM is as important from a surgical perspective.

The most commonly performed SA strategy reflects an evolution of the pioneering work of Dr James Cox whose "cut-and-sew" strategy to ablate triggering lesion sets that is now on its fourth iteration (termed "Cox-Maze IV") that involves a combination of cryoablation and RFA.[19] Both modalities are often used concomitantly and have roughly equivalent efficacy and safety, through cryoablation may be associated with superior rates of atrial contractility restoration.[20,21] A key aspect of the approach for left atrial lesions involves isolation of the LPVs and identification of the LOM, which is surgically exposed via lateralization of the heart towards the right and is divided with electrocautery.[1,22] The LPVs can then be encircled and isolated via a bipolar radiofrequency clamp. This is described as the first step in ablation of left atrial lesion sets which subsequently include the left superior pulmonary vein to left atrial appendage lesion, left atrial appendage closure, right PVI, box lesion construction, ablation of the coronary sinus lesion, mitral line ablation, and finally ablation of right atrial lesions.[22,23] It is important to note that catheter-based alcohol ablation of the LOM can be performed even after prior surgical ablation in cases of refractory AF.[24]

PV ISOLATION AND CONSIDERATIONS OF THE LOM DURING LUNG TRANSPLANTATION. SA is often performed concomitantly with other cardiac operations including coronary revascularization and valvular surgery.[25] The LOM may be a potent SA target during lung transplantation. It is important to note that bilateral transplantation and preoperative pulmonary fibrosis are independently associated with postoperative AF.[26] During the conduct of lung transplantation, the pulmonary veins are, by definition, surgically isolated.[27] Release of the LOM is an important step in developing the PV cuff when anastomosing the left lung to the left atrial cuff. It is important to note that PVI may be impacted by the length of the remnant left atrial and pulmonary venous cuff while clamping and performing the donor-recipient venous anastomosis. As such, patients undergoing lung transplantation with preoperative AF may be particularly impacted by the cuff length. In these

cases, identification of the LOM in the donor specimen prior to implantation may be of particular importance. Furthermore, preoperative AF is associated with increased risk of postoperative atrial arrythmias and increased length of stay after lung transplantation.[28] To investigate the management of preoperative AF in this setting, Xia and associates[27] recently investigated the utility of concomitant RFA-based PVI (which frequently involves LOM ablation as discussed) and left atrial ligation in a series of 61 patients. This yielded an 85% rate of freedom from death, stroke, cardiac readmission and repeat ablation at 1 year.[27] Overall, surgical PVI during lung transplantation is associated with reduced risk of postoperative late AF, particularly with bilateral implantation, and it is likely that the LOM is an important putative target during surgical PVI.[29] Further specific investigation into LOM targeting during lung transplantation is warranted. Specifically, it will be important to investigate whether intentional identification and ablation of the LOM at the time of left lung transplantation impacts incidence of postoperative AF, particularly in those patients with preexisting comorbid AF.

COMMENT

The LOM is an important therapeutic target for invasive management of atrial fibrillation, from both catheter-based and surgical approaches. While CA of AF through empiric PVI and LOM ablation is an effective initial strategy, ablation of the LOM as part of a comprehensive SA strategy is an effective strategy for refractory or recurrent atrial fibrillation. In addition to its documented efficacy and safety as a concomitant operation with other cardiac surgical cases, SA including PVI and LOM ablation is an important aspect of post-surgical AF prevention in patients undergoing lung transplantation. As the number of patients undergoing lung transplantation continues to rise, further investigation into specific ablation of the LOM during transplantation is warranted.

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