



Impact of Technique and Technology on Mitral Isthmus Ablation

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Abstract

Purpose of review Mitral isthmus ablation is an established strategy in the treatment of peri-mitral atrial flutter and as an adjunct to pulmonary vein isolation. The objective of this review is to summarize the techniques and specific strategies that allow for increased success and durability of mitral isthmus ablation.

Recent findings Achieving bidirectional block across the mitral isthmus remains a challenge due to the increased thickness in this region, convective cooling as a result of coronary sinus blood flow, and the occurrence of epicardial connections. Several strategies to achieve durable mitral isthmus block, such as coronary sinus ablation, coronary sinus balloon occlusion, ethanol ablation via the vein of Marshall, and using alternate mitral lines in select cases, are described in detail in this review.

Introduction

Mitral isthmus (MI) ablation is an established strategy in the treatment of peri-mitral atrial flutter as well as an adjunct to pulmonary vein isolation (PVI) in the treatment of persistent atrial fibrillation (AF) [1, 2]. Luria et al. first described left atrial (LA) “isthmus” in patients undergoing ablation for left lateral accessory pathways. They noted the

occurrence of intra-atrial conduction block in a subset of these patients, which was ascribed to inadvertent damage to a narrow “isthmus” of myocardium between the lateral mitral annulus and the left inferior pulmonary vein (PV) [3]. Multiple hypotheses have been proposed to explain the therapeutic efficacy of mitral isthmus ablation during

AF ablation. These include the elimination of anatomic or functional reentry involving the MI and/or left-sided pulmonary veins, organization of AF to a macroreentrant peri-

mitral atrial flutter during pulmonary vein isolation, and targeting the ganglionated plexus that is located along the inferolateral aspect of the posterior LA [4].

Anatomical aspects of the mitral isthmus

The mitral isthmus is traditionally defined as the portion of the left atrial wall constrained between the mitral valve annulus and the orifice of the left inferior pulmonary vein (Fig. 1a). However, this terminology does not encompass the multiple anatomically discrete ablation targets that have been proposed, which are able to disrupt the corridor of conducting tissue between the mitral annulus and the left pulmonary veins [5]. These targets include alternate “lines” such as the right superior pulmonary vein (PV) to the mitral annulus (anteromedial line), the left superior PV to the mitral annulus, and a line similar to the classic MI line except

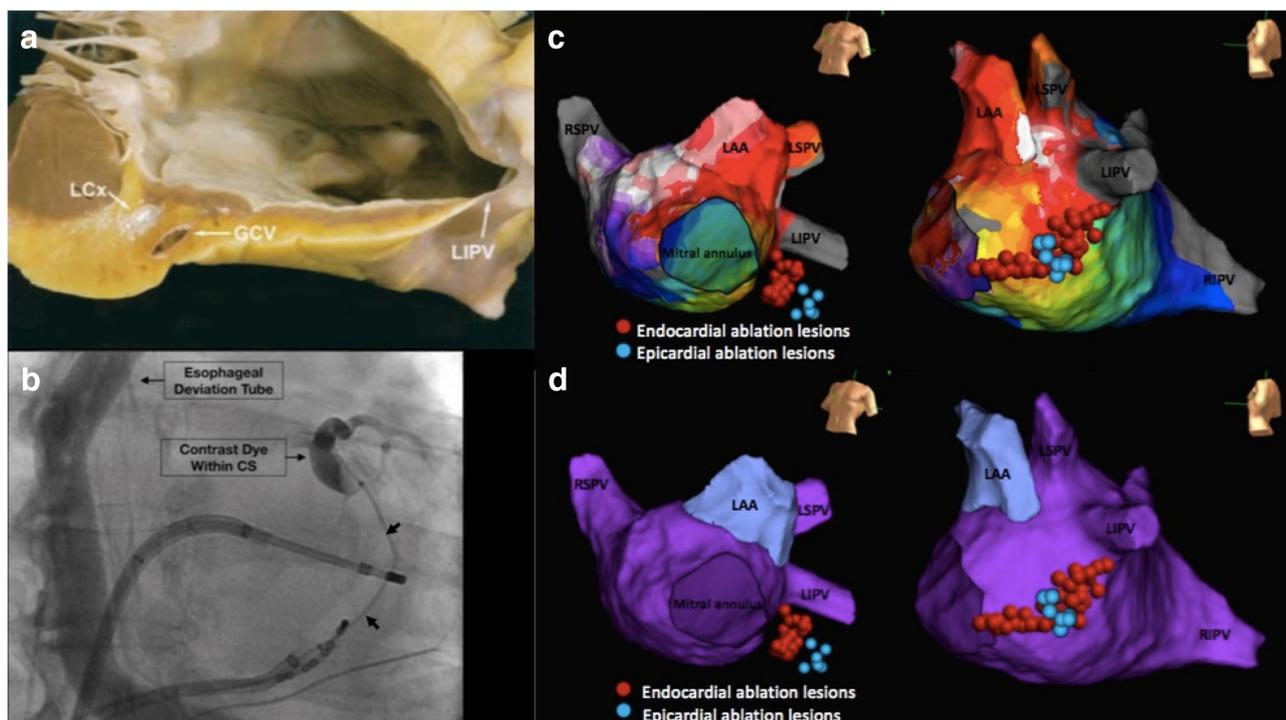


Fig. 1. Mitral isthmus anatomy and ablation. **a** Anatomical aspects of the mitral isthmus between the left inferior pulmonary vein (LIPV) and the mitral valve (MV). **b** Endocardial mitral isthmus ablation with coronary sinus (CS) balloon occlusion with air (short black arrows). **c** Activation map of peri-mitral flutter with endocardial (red tags) and epicardial lesion set (blue tags) in the left atrium. **d** Endocardial mitral isthmus ablation with a lateral mitral isthmus line (red tags) and circumferential ablation within the coronary sinus (blue tags).

GCV, great cardiac vein; LAA, left atrial appendage; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein. Panel **a** is obtained from Becker et al, *J Cardiovasc Electrophysiol* 2004; 15:809–812. Panel **b** is obtained from Pathik et al, *HeartRhythm* 2019; 16(4):632–637.

that the line course is closer to the base of the LAA. The myocardial thickness is highly variable at the MI level ranging from 1.2 to 7.7 mm [5, 6].

On the epicardial surface of the MI, the coronary sinus is an important structure to be considered as it courses along the inferior left atrial wall approximately 1 cm above the mitral valve annulus. The importance of this structure from a perspective of providing an epicardial connection across the MI and its heat sink effects that impact endocardial ablation will be discussed later. The ligament of Marshall is yet another epicardial structure along the ridge between the LA appendage and left PV. The ligament of Marshall contains the vein of Marshall (VOM) and autonomic nerves within a venous sleeve called the Marshall bundle (MB). The vein of Marshall (VOM) is the remnant of the left superior vena cava and drains into the coronary sinus at the same end as the great cardiac vein, marking the origin of the coronary sinus [7]. This is an important structure as it has been implicated as a trigger of AF, a source of arrhythmogenic autonomic innervation, and an electrical connection between the left pulmonary vein and neighboring myocardium [8, 9]. The MB may have variable connections to the CS musculature and the LA, which may prevent conduction block with MI ablation.

Importance of achieving bidirectional block

The feasibility of MI ablation using the classic approach, i.e., connecting the left inferior pulmonary vein (LIPV) to the lateral mitral annulus, was first prospectively studied by Jais et al. [2]. Although the mitral isthmus is relatively short (average of 35 mm and ranging between 15 and 52 mm), bidirectional block is difficult to achieve by endocardial ablation only [10]. Jais et al. and Fassini et al. reported complete conduction block in 92 and 76% of patients, respectively [2, 11]. A significantly high number of patients (68% in Jais et al. and 75% in Fassini et al.) required RF delivery from within the coronary venous system emphasizing the difficulty in achieving complete conduction block. Subsequent studies by Hocini et al. demonstrated conduction MI block in only 68% of patients despite CS occlusion [12]. Failure to achieve bidirectional block with MI ablation cannot be underestimated as it has been shown to be pro-arrhythmic [13]. In fact, incomplete linear lesions in patients who undergo substrate modification along with PVI in persistent AF have increased recurrence of AF and LA flutter [14]. Other investigators have reported recurrent atrial flutters as high as 11% in patients with incomplete mitral isthmus lines [11]. In a single-center study by Barkagan et al., there was increased frequency of inducible arrhythmias in patients with residual conduction over the mitral isthmus line compared to patients with complete mitral isthmus block (63.6 vs. 30%) [15]. All these data point to the importance of proving bidirectional block acutely as well as using techniques that ensure that these lines will be durable in follow-up.

Challenges associated with mitral isthmus ablation

It is well-recognized that MI ablation is challenging from both an efficacy and a safety standpoint as it may be associated with significant complications. The diversity in anatomy and the neighboring anatomical structures (as described previously) limit the ease with which we can achieve bidirectional block with linear ablation (almost exclusively done with point-by-point RF). Detailed

description of some of the important challenges associated with MI ablation is presented subsequently.

Challenges in thickness

Becker et al. observed a wide variation of myocardial thickness ranging from 1.4 to 7.7 mm at the level of the LIPV, at 1.2 to 4.4 mm in the mid-isthmus region, and up to 3.2 mm at the mitral annulus, respectively [5]. In terms of the various positions along which the mitral isthmus can be ablated, the maximal myocardial thickness was found to be greatest over the anterolateral mitral line (from left superior PV to the 12 o'clock position on the mitral annulus). Another approach used for MI ablation is to target the anteromedial mitral line (right superior pulmonary vein to 10 o'clock position on the mitral annulus), but imaging studies have noted that ridges and diverticuli were found most frequently at this site [16].

Heat sink

Epicardial vascular structures, such as the coronary sinus (CS) and circumflex artery near the mitral annulus, can reduce conductive heating of the subepicardium and act as "heat sink," thereby limiting lesion transmuralty [6]. The CS blood pool, in particular, attenuates convective cooling to a lesser extent if "static" by proximal occlusion or "displaced" by a poor thermal conductor (described in subsequent texts). A larger CS diameter has been shown to be associated with need for CS ablation as well as increased ablation time in order to achieve an effective block [17].

Left circumflex artery

Operators have reported close proximity of the left circumflex artery to the CS (<2 mm from the CS catheter) at the lateral and anterolateral mitral annulus in 24% of patients [18]. The incidence of coronary artery injury has been estimated at 1 in 499 patients during CS occlusion in a single-center study. The low incidence is likely attributed to the convective cooling by the CS blood flow [19]. Ablation within the CS, close proximity of the left circumflex artery and CS, and a small caliber distal circumflex were found to be risk factors for circumflex artery injury in a study looking at post-CS ablation coronary angiography. Although the incidence of asymptomatic coronary artery injury (stenoses ranging from 50 to 80%) was high (28%), all of them resolved with intracoronary nitrates suggesting that the mechanism was thermal-mediated vasospasm [20]. In addition, an interposed left circumflex artery between the CS and MI is an independent predictor of failure to achieve MI block [10, 21].

Epicardial bridges

Myocardial sleeves around the CS and the vein of Marshall (VOM) as described previously may act as epicardial bridges preventing MI block despite endocardial ablation. The coronary sinus has a continuous cuff of muscle of variable thickness (ranging from 0.3 to 2.5 mm) surrounding the venous wall of the CS and extending a variable distance from the CS ostium (mean at 40 ± 8 mm) [22]. Hence, endocardial ablation alone may result in a local block which is bypassed by ongoing epicardial conduction resulting in recurrent peri-mitral tachycardia [23]. The occurrence of epicardial connections was further

supported by high-density activation mapping in a prospective study of 56 patients undergoing MI ablation. These epicardial bridging connections insert over the proximal–middle coronary sinus laterally and the left atrial ridge medially with an average distance of 2.4 ± 1.6 cm from the MI line [15].

Ablation techniques

There are several different strategies for MI ablation to overcome the challenges listed previously.

Standard technique

LA endocardial ablation

The standard technique for endocardial MI ablation is to create a linear ablation line connecting the LIPV to the lateral mitral annulus. The sheath-catheter apparatus is positioned along the lateral mitral annulus, and the catheter is positioned with an atrioventricular ratio of 1:2 at the lateral mitral annulus. We prefer a 3.5-mm irrigated force-sensing ablation catheter using a steerable sheath to ensure adequate tissue contact and catheter stability with “point-by-point” ablation guided by 3D electroanatomical mapping. Initial endocardial ablation settings typically range from 35 to 50 W with durations between 30 and 60 s given the thick myocardial substrate along the line. Radiofrequency ablation is titrated to impedance with preference for higher power near the annular end of the mitral isthmus.

More recently, high-density electroanatomical mapping has been found to be helpful in patients with peri-mitral flutter by often demonstrating narrow areas of constrained activation/slow conduction in regions of the scar. In such patients, the flutter can be terminated at the critical isthmus away from the MI location and alternative lines may be considered.

Epicardial LA ablation

Despite endocardial mitral isthmus ablation, between 48 and 97% of patients have reported to need epicardial ablation within CS to achieve complete block [24–26]. In the CS, the catheter should be deflected towards the atrial tissue opposite to the lesions delivered endocardially and care should be taken to avoid distal CS ablation which increases the risk of left circumflex artery injury. It is recommended to commence energy delivery at low powers (15–20 W) with careful up-titration and avoiding both impedance rises and excessive impedance drops. Additional circumferential lesions at or distal at site of ablation may be needed to achieve complete mitral isthmus block. Operators have recommended circumferential ablation within the CS using short-duration lesions with low flow (2 mL/min) to avoid lesion sparing [27•] (see Fig. 1c,d).

CS balloon occlusion

As previously discussed, CS blood flow attenuates thermal conduction from an endocardial heat source. Although operators have attempted occluding the proximal CS to reduce conductive cooling by creation of a static blood pool,

displacement with an air-filled balloon has been found to be superior [27•, 28]. D'Avila et al. first demonstrated lesion transmuralty after temporary CS occlusion using a 30-mm-long CS balloon catheter inflated with air in a porcine study [29]. In a randomized study of 46 patients, CS balloon occlusion using a 4.0×10 mm or 2.0×10 mm PTA dilatation catheter significantly decreased the need and duration of epicardial CS ablation (48 vs. 83%). However, there was no significant difference in the acute success rate compared to patients without CS balloon occlusion [28]. Other operators have used a 1-cm spherical Swan-Ganz balloon but have not demonstrated significant differences in CS ablation times. Therefore, this approach is not used clinically [12]. One of the reasons may be that due to the shorter profile, the Swan-Ganz catheter displaces blood from a shorter CS segment and is therefore less effective [12]. More recently, Pathik et al. have described their institutional approach for mitral isthmus ablation [27•]. They recommend using a SL-2 sheath (Abbott Inc., Abbott Park, IL), which is then replaced by a 8–10 mm \times 40 mm vascular balloon over the guidewire into the CS and adjacent to the planned ablation site. CS balloon occlusion is performed by inflating the balloon with air, and contrast injection is used to confirm CS occlusion [27•] (see Fig. 1b).

VOM ablation

The proposed methods for VOM ablation are endocardial ridge ablation, radiofrequency ablation inside the VOM, and ethanol infusion into the VOM. Radiofrequency ablation along the high lateral ridge has been shown to be useful by targeting the VOM endocardially in cases of apparent bidirectional MI block [30]. However, ridge ablation may not always be successful to achieve mitral block given multiple MB-LA connections, and, more recently, ethanol ablation of VOM has gained popularity [31]. Valderrabano et al. have demonstrated the mechanistic role of the VOM in the peri-mitral circuit with entrainment maneuvers and the successful treatment by ethanol infusion in achieving MI bidirectional block [32, 33].

From a procedural standpoint, the VOM can be identified as the posteriorly directed atrial branch of the CS in a right anterior oblique projection after an occlusive CS venogram. Some operators have cannulated the VOM using a quadripolar catheter (1.7 F Pathfinder Mini, Cardima, or 4 F IBI, St. Jude Medical, Minneapolis, MN) which may help in entrainment and activation mapping. Another approach is to sub-selectively cannulate the VOM with a 0.014-in. guidewire preloaded over the wire balloon through an angiographic catheter [27•]. The angioplasty balloon is inflated into the VOM, and, following a selective VOM venogram, 100% ethanol is administered into the VOM via the angioplasty balloon [27•]. Operators have used up to one to four balloon injections of 1 mL 98% ethanol depending on the length of the VOM [33].

Alternative mitral isthmus lines

Alternative approaches to the mitral line have been proposed given the difficulty in achieving bidirectional block and the potential for injuring the left circumflex artery. The anteromedial mitral line (right superior pulmonary vein or right inferior pulmonary vein to 10 o'clock position on the mitral annulus) is an alternative but maybe less favorable due to the increased myocardial thickness, longer isthmus, and the greater percentage of ridges, which make

contiguous, transmural ablation difficult to achieve [34]. The superolateral line on the other hand involves creating a linear lesion from the posterior base of the LAA orifice adjacent to the left superior pulmonary vein (LSPV) to the mitral annulus. Operators have described reduction in the need for CS ablation with this approach; however, there is a higher risk of cardiac tamponade given the thin atrial myocardium over the superolateral aspect of the LA [35]. Alternatively, a modified anterior line (anterior aspect of the LAA connected to the LSPV continued to the anterolateral mitral annulus) is a safer and effective alternative approach with a reported 88% acute success rate in achieving bidirectional MI block [36].

Other approaches

Investigators have described the need for subxiphoid epicardial access as an approach after unsuccessful endocardial and CS ablation. However, the risks of epicardial access along with coronary artery and phrenic nerve injury need to be considered [37] and alternatives, such as CS balloon occlusion and VOM alcohol injection, should be performed before this approach is considered.

Testing for bidirectional block

After completion of the ablation line, a variety of strategies can be utilized to confirm bidirectional block, including differential pacing and high-density electroanatomical mapping. Pacing from either side of the line with pacing catheters positioned as close as possible to the line followed by measurement of trans-isthmus conduction time, documenting widely spaced double potentials along the line, and reversal of the coronary sinus (CS) activation pattern during pacing from the septal (anterior) side of the ablation line are used to confirm mitral isthmus block. However, slow endocardial conduction through the isthmus or the presence of epicardial bridging connections with insertion sites distant from the line may lead to falsely prolonged trans-isthmus conduction time accompanied by only partial reversal of CS activation [38–40]. High-density activation mapping of the endocardium and epicardium can help determine the block and is especially helpful in cases of recurrent peri-mitral tachycardias [15•].

Conclusion

Achieving bidirectional block across the mitral isthmus remains a challenge despite the use of improvements in both technology and tools and is not an infrequent issue encountered in clinical practice. Some of the challenges include the thickness of the myocardium in these regions, convective cooling as a result of coronary sinus blood flow, and the occurrence of epicardial connections. Specific strategies that allow for increased success and durability of this line include the use of CS ablation, CS balloon occlusion, ethanol ablation via the VOM, and finally using alternate mitral lines in select cases. Several newer technologies, such as RF catheters with large tips that allow for the use of high powers and pulse field ablation, show promise in their ability to achieve these goals in a safe and efficient manner, and further studies are needed to better understand what role these will play in the future.

Compliance with Ethical Standards

Conflict of Interest

Aditi Naniwadekar and Jacob Koruth declare that they have no potential conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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