Electrical connections between left superior pulmonary vein, left atrium, and ligament of Marshall: implications for mechanisms of atrial fibrillation

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Tan, Alex Y., Chung-Chuan Chou, Shengmei Zhou, Motoki Nihei, Chun Hwang, C. Thomas Peter, Michael C. Fishbein, and Peng-Sheng Chen. Electrical connections between left superior pulmonary vein, left atrium, and ligament of Marshall: implications for mechanisms of atrial fibrillation. Am J Physiol Heart Circ Physiol 290: H312–H322, 2006. First published September 9, 2005; doi:10.1152/ajpheart.00369.2005.—The importance of the ligament of Marshall (LOM) to rapid activations within the left superior pulmonary vein (LSPV) during atrial fibrillation (AF) remains poorly understood. We aimed to characterize the importance of electrical coupling between the LSPV with the left atrium (LA) and the LOM in the generation of high-frequency activations within this PV. We performed high-density mapping of the LSPV-LA-LOM junction in eight dogs, using 1,344 electrodes with a 1-mm resolution before and after posterior ostial ablation to diminish PV-LA electrical connections. A LOM potential was recordable up to 6.5 mm (SD 2.2) into the LSPV in all dogs during sinus rhythm (SR) and LA pacing. Functional LOM-LSPV electrical connections bypassing the PV-LA junction were present in five of eight dogs. Direct LOM-LSPV connections contributed to 46.5% (SD 16.0) of LSPV activations during AF, resulting in a higher propensity to develop focal activations (P < 0.05) and a higher activation rate during AF of LSPVs with direct LOM connections compared with those without (P < 0.03). Posterior LSPV ostial ablation without damaging the anterior wall or LOM slowed residual LA-PV conduction (P < 0.001). This diminished PV-LA coupling prevented the reinduction of LSPV focal activations in all dogs. However, persistent LOM focal activations in two dogs continued to activate the LSPV rapidly [cycle length 151.8 ms (SD 4.8)] via direct LOM-LSPV connections. LOM-LSPV connection forms an accessory pathway that contributes to the electrical coupling between LSPV and LA during SR and AF. This pathway may contribute to rapid activations within the LSPV during AF.

Rapid activations within the pulmonary veins (PVs) are important in the mechanisms of atrial fibrillation (AF). The left superior (LS) PV is a frequent source of these rapid activations during AF (5). The potential role of the ligament of Marshall (LOM) in contributing to rapid activations within the LSPV remains unclear. Rapid activations within PVs during AF may be due to both reentrant excitations involving the PV and the left atrium (LA) and focal discharges arising from within the PVs themselves (1, 14). A possible mechanism for focal discharge is afterdepolarizations and triggered activity. Hence, the ability to rapidly activate PV (2) may promote triggered activity and focal discharges. Improved PV-LA communications may therefore be essential for the generation of PV focal discharges (10) by allowing the PV and the LA to reciprocally activate each other rapidly during AF. However, it is known that PV-LA muscles are frequently discontinuous (6), limiting the extent of PV-LA electrical connections. Therefore, the presence of an additional connection between the PV and the LA bypassing the PV-LA junction may improve PV-LA electrical connections and contribute to rapid activations within the PV. The muscle tract (Marshall bundle, MB) within the LOM may directly connect the coronary sinus (CS) muscle sleeve to the LA (8). In addition, anecdotal cases suggest that the LOM also connects directly with the LSPV (9). If the latter is correct, the LOM may serve as an accessory pathway for LSPV activation that bypasses the PV-LA junction. This may lead to improved electrical coupling between the PV and the LA, with potential implications for PV arrhythmogenesis (7). However, definitive proof of direct LSPV-LOM connections from high-density mapping or pathological studies is lacking. The purpose of the study was to perform high-density epicardial mapping (1-mm resolution) of the canine LSPV-LA-LOM junctions to 1) demonstrate that the MB within the LOM may serve as an accessory pathway that connects the LA to the LSPV during both sinus rhythm (SR) and AF and 2) test the hypothesis that this accessory LA-LSPV pathway maintains rapid communications between the LSPV and the LA even when the direct PV-LA connection is decreased by segmental posterior ostial ablation.

MATERIALS AND METHODS

The research protocol was approved by the Institutional Animal Care and Use Committees of Cedars-Sinai Medical Center and conforms to American Heart Association guidelines. We studied eight normal dogs (22–27 kg).

Electrophysiological Study and Mapping

We performed a median sternotomy under isoflurane anesthesia. Bipolar hook electrodes were attached to the left atrial appendage (LAA) and connected to Prucka Labsys for epicardial pacing and recording. We paced the LAA at decremental cycle lengths (CLs; 400, 300, 200, 150 ms), performing high-density mapping of the anterior and posterior aspects of the LSPV-LA junction at each CL. We defined anterior LSPV-LA junction as the half of the junction closest to the LAA and posterior LSPV-LA junction as the half diametrically opposite to the anterior junction and closest to the posterior LA (6).
Two multielectrode plaques each with 1-mm electrode resolution were connected to a UniMap (Auckland, New Zealand) mapping system. The first plaque (448 bipolar electrodes over 28 mm × 16 mm) was used to map the epicardial posterior aspect of the LSPV and the second plaque (896 bipolar electrodes over 28 mm × 32 mm) to map the epicardial anterior aspect of the LSPV, adjoining the LA and distal half of the LOM. Figure 1 shows the experimental preparation. The red box in Fig. 1A shows the anterior mapping field. Figure 1B shows the position of the posterior mapping plaque (green box), which was inserted behind the PV. Because exposure was via a median sternotomy, the posterior LA was not directly visualized. Instead, the posterior aspects of the LSPV and LSPV-LA junction were blunt dissected free from the surrounding mediastinal tissues, so that the mapping plaque could be appropriately positioned as shown in the inset in Fig. 1B.

Anatomically the LSPV-LA junction was identified by the concavity that separates the LSPV from the LA. This is indicated by the dashed line in Fig. 1A. Because the PV tissues were fragile, the plaques were not sutured onto the PV. To prevent undue movement during data acquisition, the plaques were gently held in place against the tissue. To ensure that there was no shift in plaque position, specific anatomic landmarks, such as the outlines of the LSPV and the position of the PV-LA junction, were marked on the back side of the plaque with indelible ink and the plaque position was constantly checked against these landmarks. Because the mapping plaques were flexible and could easily accommodate the curvatures of the tissues, adequate contact of the plaque with the LA-LSPV junction was possible to ensure accurate mapping of this region. Each high-density recording was 4 s long. After baseline mapping, we induced AF [36.0-s (SD 9.4) duration] by burst LAA pacing (10-s bursts, 3 times diastolic threshold, 50-ms CL, repeated up to 3 times) and repeated high-density mapping.

**Ablation**

On completion of baseline mapping, we performed epicardial radio frequency (RF) ablation at the posterior PV ostium. The purpose of this procedure was not to specifically achieve electrical isolation of the LSPV but to examine the changes in conduction patterns between the LA, LSPV, and LOM in the setting of reduced LA electrical input into the LSPV. We showed previously (6) that in canines PV-LA muscular connections in the posterior junction are more robust than in the anterior junction. Therefore, we hypothesized that ablation of the posterior junction alone is able to significantly reduce PV-LA electrical connections. In this setting, therefore, the contribution of direct LOM electrical input into the generation of LSPV rapid activations could be better discerned. We used a hand-held 4-mm-tip ablation catheter to deliver epicardially, under direct vision, RF energy that averaged 30 s per application, at 20–30 W. The anterior LSPV-LA junction and the LOM were avoided. High-density mapping was repeated to ensure that the end point of ablation, defined as the elimination of all PV activation on the posterior map, was reached. After epicardial ablation, the same mapping and pacing protocol was repeated. The dog was then euthanized.

**Histological Analyses**

The hearts were fixed in 4% formalin for 1 h and stored in 70% alcohol. PVs were sectioned longitudinally into anterior and posterior segments or in cross sections, paraffin embedded, cut into 5-μm sections, and finally stained with hematoxylin and eosin for light microscopy.

**Data Analyses**

**LA-PV interval.** The anterior PV-LA junction was first identified on the isochronal map. Because the junction is frequently the site of conduction block/delay (6), it corresponds to the region with close isochronal lines between the PV and the LA. In this location, complex double or fused potentials could be identified along the junction. The width of the junction was ~1–1.5 cm. Five contiguous bipolar electrodes along the middle portion of the junction were selected from the epicardial mapping array. For each electrode, the LA-PV interval is the interval between atrial and PV activation. LA-PV interval was measured during drive LA pacing at decremental CLs from 400 to 150 ms. Because the beats were identical during pacing, two beats were chosen for each electrode and the mean was obtained. The LA-PV interval for each pacing CL was calculated from the mean interval from those five electrodes.

**Decremental conduction.** Decremental conduction was defined as the rate-dependent increase in LA-PV interval during drive cycle (3). We analyzed AF patterns on high-density mapping, using methods reported previously (14). Briefly, a focal discharge is defined as an activation that spreads outward in all directions.

Data were expressed as means (SD). Values between two groups were compared with Student’s two tailed t-tests, and values at different pacing intervals were compared with ANOVA, followed by Newman-Keuls post hoc analysis. A 2 × 2 χ²-test was used for nonparametric comparisons between PVs with LOM connections and those without. A P value of ≤0.05 was considered statistically significant.

**RESULTS**

**LSPV-LOM Connection**

Using high-density mapping, we observed that the electrical activity in the LOM propagated to its distal end located 6.5 mm (SD 2.2) beyond the LSPV ostium in all dogs. At the distal end

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**Fig. 1.** Experimental preparation. A: anterior mapping field. B: posterior mapping field. Inset shows the posterior plaque when placed in position. LSPV, left superior pulmonary vein; LSPV1 and -2, branches of LSPV; LIPV, left inferior pulmonary vein; LAA, left atrial appendage; LOM, ligament of Marshall; LAA, left atrial appendage.
of the LOM, there were functional electrical connections between the muscle sleeves of the LOM (or MB) and the LSPV beyond the LA-PV junction in five of eight dogs. In the other three dogs, LOM electrical activity terminated beyond the LA-PV junction in a blind end.

**LOM-LSPV Connections During Paced Rhythm**

Figure 2 shows high-density mapping of the LOM-LSPV-LA junction during LAA pacing (150-ms CL). It illustrates two points, first, the presence of a direct LOM-LSPV electrical connection (Fig. 2, A–C) and second, the presence of an anatomic connection between the LSPV and LOM bypassing the LA-PV junction (Fig. 2, D–F). During LAA pacing, wave front propagated from LA into LSPV and from LSPV into the LOM (Fig. 2A, curved arrow; Fig. 2B, 44 ms). The electrogram at that time showed fused LOM and PV potentials (Fig. 2C, electrogram d). The wave front then propagated retrogradely along the LOM (Fig. 2B, 44–61 ms) and collided with another wave front originating from the proximal LOM close to the CS (Fig. 2B, 83 ms), generating double LOM potentials (Fig. 2C, electrogram g) at that point. This finding indicates the presence of direct LSPV-MB connections that bypassed the LA-PV junction. In Fig. 2D, a histological cross section was obtained at site 1; it should be noted that this site was beyond the LA-PV junction. Figure 2E shows that there is an anatomic connection between the muscle sleeves of the LOM (MB) and anterior wall of LSPV beyond the LA-PV junction. Figure 2F is a higher-power view of this connection.

**LOM-LSPV Connection During AF**

Figure 3 shows LOM-LSPV electrical connections during AF. It illustrates two points: 1) there are direct LOM-LSPV electrical connections during AF, and 2) LOM focal discharges and LOM nonfocal activations can both contribute to rapid LSPV activations during AF via LOM-LSPV connections. Figure 3A illustrates the anterior mapping field (a–h indicate electrograms displayed in Fig. 3D). Activations at the LSPV-LA junction were more rapid than that in the LA, as illustrated by Fig. 3B. An expanded view of the segment underlined by the bar and asterisk in Fig. 3B shows that the PV-LA junction electrogram consisted of both LOM (letter m) and fused PV-LA activations (letter va). This finding indicates that LOM activation accounted significantly for the rapidity and complexity of activations observed at the LSPV-LA junc-

**Fig. 2.** Electrical and anatomic connections between the LOM and the LSPV. A: isochronal map during LAA pacing. Schematic diagram shows location of electrograms as displayed in C. B: dynamic activation sequence of the same beat as that shown in A. Numbers are times (in ms), with 0 being the earliest activation on the map. D: photo of the mapped area. Site 1 indicates the histological section shown in E and F. F is a high-power view of the box in E. s, Stimulus artifact; N, nerves; MB, Marshall bundle.
tion. Figure 3C shows isochronal maps from four beats (1–4 on the PV-LA junction electrogram in Fig. 3). During AF, intermittent focal discharges from two separate sources were present in this preparation. One was from the LOM (arrowhead, Fig. 3C, beat 2), and the other from the LSPV (dagger, Fig. 3C). These focal discharges sometimes coincided (beat 2) and sometimes did not (beat 4). There were two types of LOM activation patterns that contributed to rapid LSPV activations. The first pattern was of LOM focal discharge (beats 2 and 4). In beat 2, both LOM focal discharge and PV focal discharge were observed. LOM focal discharge propagated distally into the LSPV and also retrogradely toward the CS and LA. This LOM focal discharge excited the LSPV1 branch of the LSPV, whereas the other branch (LSPV2) was activated mainly by its own focal source. In beat 4, only LOM focal discharge was observed. Therefore, intermittent bursts of LOM and PV focal discharge together contributed to rapid LSPV activations during electrically induced AF. Beats 1 and 3 show LOM nonfocal activations. In these two beats, LOM wave front propagated from proximal LOM close to the CS (outside field of view) to the distal LOM close to the LSPV. This wave front subsequently activated the LSPV via direct LSPV-LOM connections located beyond the LSPV-LA junction. After this, the wave front from the LSPV propagated across the LSPV-LA junction to activate the LA. These data show that the LOM can serve as an accessory pathway between the CS and the LSPV, bypassing the LA.

We successfully induced 31 episodes of AF from 7 of 8 dogs with the method described above. Twenty-four of these episodes were mapped in high density. Five of these seven dogs (n = 14 episodes) had demonstrable electrical LOM-LSPV connections during AF. In these 14 episodes of AF from 5 dogs, 5.7 wave fronts/s (SD 1.0) were observed to reach the LOM-LSPV connection point. However, only 3.9 wave fronts/s (SD 1.6) [62.6% (SD 11.4)] established successful...
LSPV-LOM electrical connections. In the rest, the wave front was blocked as it approached the target that had been activated <50 ms earlier and was hence refractory [LSPV effective refractory period (ERP) 108.6 ms (SD 19.5)]. In this case, the PV could have been preactivated either by LA wave fronts or by its own focal source. Alternatively, LSPV activations may fail to propagate to the LOM because of collision with a LOM wave front approaching from the opposite direction. Of 7.8 LSPV activations/s (SD 0.5) during AF, 3.6 activations/s (SD 1.2) [46.5% (SD 16.0)] were contributed partially or totally by the LOM. LSPV focal activations were inducible in five of five LSPVs with functional LOM-LSPV connections compared with one of three LSPVs that did not have LOM-LSPV connections (P < 0.05). Activation CLs during AF of LSPVs with functional LOM-LSPV connections were 117.2 ms (SD 15.8; n = 5), compared with 168.5 ms (SD 47.2; n = 2) for those without functional LOM connections (P < 0.05). For the third LSPV without LOM connection, that dog did not have inducible AF. However, rapid LA pacing at 100-ms CL in that dog activated the LSPV at a slow CL of 233.3 ms (SD 28.9; n = 3 episodes) because of conduction block at the LA-PV junction. These data indicate that 1) LOM focal and nonfocal activations both contribute to rapid activations within the LSPV via direct LOM-LSPV connections and 2) the LOM may form an additional connection between the LA and the LSPV that allows wave fronts to bypass the LA-PV junction.

LA-PV Electrical Connections

Complex LA-PV propagation patterns and decremental conduction. Figure 4 shows complex LA-LSPV electrical connections during SR (Fig. 4, A–C) and the changes in conduction patterns that result from posterior ostial ablation (Fig. 4, D–F). Figure 4, A and D, are isochronal maps constructed from atrial/PV electrogram a enclosed by the rectangle in Fig. 4, B and E, respectively. It should be noted that the purpose of this figure is to show the changes in LA-LSPV conduction patterns with posterior LSPV ostial ablation. Therefore, the LOM potential indicated by m in Fig. 4, B and E, was excluded from the isochronal map. The schematic drawings in Fig. 4, B and E, summarize the respective conduction patterns. Before posterior ostial ablation (Fig. 4, A–C), the activation patterns of the LSPV were complex. Figure 4A shows that anterior LSPV was activated by LA wave fronts that propagated across the anterior LA-PV junction as indicated by electrograms a to b and e to f in Fig. 4C. In addition, it was also activated by wave fronts that

![Fig. 4. LA-PV conduction patterns during sinus rhythm (SR) before (A–C) and after (D–F) posterior ostial ablation at the LA-PV junction (LA-PVJ). A and D: isochronal maps of anterior and posterior LSPV. B and E: Only atrial/PV electrogram a was selected for isochronal map construction. C and F: electrograms from various locations (a–p) selected to indicate the presence of complex LA-PV conduction. Numbers above each electrogram indicate local activation time (ms), with 0 being the earliest activation on the anterior map.](http://ajpheart.physiology.org/)

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first appeared around the edges of the distal PV. These wave fronts then propagated retrogradely (Fig. 4C, electrograms d to c, h to g). Because these wave fronts did not appear to arise from the anterior junction, they were most likely due to propagation from the posterior surface of the PV and posterior LA-PV junction. In Fig. 4C, the numbers above each electrogram indicate the time of local activation, with time 0 being the earliest activation appearing on either anterior or posterior map. The data in Fig. 4C indicate that during SR before ablation activation appeared earlier in the posterior PV (earliest 11 ms, Fig. 4C, electrogram m) than anterior PV (earliest 14 ms, Fig. 4C, electrogram d). Overall, activation appeared earlier in the posterior PV by 3.2 ms (SD 1.8) compared with the anterior PV in all dogs. This implies that LA-PV conduction across the posterior junction was marginally faster than that across the anterior junction. Similarly complex patterns were observed in all dogs, during both SR and LAA pacing. Therefore, we performed posterior ostial ablation instead of anterior ostial ablation because the above finding suggested that propagation across the posterior junction was faster than that across the anterior junction. We hypothesize therefore that posterior ostial ablation will significantly reduce LA-PV electrical connections.

Figure 4, D–F, illustrates the changes in conduction patterns after posterior ostial ablation at the LA-PV junction. Posterior PV activation was eliminated (Fig. 4D), and electrograms in the posterior map (Fig. 4F, electrograms l-p) showed far-field atrial activity only. Although care was taken to avoid ablating the anterior PV ostium, there was now partial anterior PV entrance block (electrograms c to d, g to h). Where anterior segmental LA-PV conduction breakthrough occurred, such as in LSPV2, the pattern of activation had become simplified, because conduction now occurred solely through the anterior junc-

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**Fig. 5.** Decremental conduction and the effects of posterior ostial ablation on conduction across the unablated anterior junction. A: isochronal maps during LA pacing [150-ms cycle length (CL)] before and after posterior ostial ablation. B: electrograms obtained from 1 location (indicated by asterisk on isochronal maps). C: LA-PV interval increases with more rapid rates of pacing (incremental conduction). After posterior ostial ablation, conduction across the unablated anterior junction is significantly slowed.
tion. This resulted in significant slowing of the PV activation, as indicated by comparison of isochronal maps in Fig. 4, D and A, and by comparison of the relative activation times of the PV in Fig. 4, F and C. The data indicate that posterior ostial ablation was able to significantly reduce LA-PV electrical connection.

Figure 5 illustrates that posterior ostial ablation was able to slow LA-PV conduction across the unablated anterior junction. Figure 5A shows activation patterns before and after ablation at the anterior LA-PV junction during LA pacing. Although anterior PV was unablated, conduction across the anterior junction was significantly slowed, resulting in greater activation delay of the PV (Fig. 5A), wider separation of atrial and PV potentials (Fig. 5B), and significant increases in LA-PV interval (Fig. 5C). Figure 5 also demonstrates the presence of frequency-dependent decremental conduction properties across the LA-PV junction before and after ablation. Figure 5, B and C, show that as activation rates increased, LA-PV propagation became increasingly slower, as indicated by increases in LA-PV intervals (Fig. 5C). At CLs below 150 ms, intermittent conduction failure resulted. This property of decremental LA-PV conduction limits the extent of functional electrical connections between PV and LA at high activation rates. The presence of additional connections between PV and LA that bypass the junction, such as that conferred by direct LOM-LSPV connections, may therefore help to improve PV-LA electrical coupling.

Role of Atrial Input in PV Focal Activation

Figure 6 illustrates the effect of diminished PV-LA electrical coupling created by posterior ostial ablation on the generation of PV focal activations by rapid LA pacing. Figure 6A shows an example of AF induction. Figure 6B shows the activation patterns in the anterior and posterior LA-PV junction during AF at the time marked by an asterisk in Fig. 6A. Before ablation (Fig. 6A), LA-PV connection was more robust. Therefore, burst LA pacing was able to capture the PV rapidly. This resulted in the initiation of fractionated high-frequency activity at the point marked by the red arrow in Fig. 6A. The isochronal map of the beat marked by the black asterisk in Fig. 6A shows that this high-frequency activity was consistent with focal activation, in this case from two discrete sites (red stars in Fig. 6B). After posterior ostial ablation, persistent anterior conduction was still observed; however, because of diminished PV-LA electrical coupling (Fig. 6C), LA wave front was unable to activate PV as rapidly as before. The reduced PV activation rate was associated with an absence of PV focal activation (Fig. 6D).

At baseline, we induced 31 episodes of AF [CL 141.8 ms (SD 12.2) measured at the LAA] from 7 dogs. Four episodes were >2 min and terminated by burst pacing. The rest averaged 36.0 s (SD 9.4) in duration and terminated spontaneously. High-density mapping was performed in 24 of 31 episodes. We observed focal activations from the anterior surface of the LSPV (Fig. 6B) in 20
episodes from 6 dogs [CL 115.5 ms (SD 13.5)] and from the LOM (Fig. 3C) in 12 episodes from 4 dogs [CL 125.1 ms (SD 9.6)]. In one dog, nonsustained AF [3 episodes, CL 158.3 ms (SD 2.8), duration 43.6 s (SD 39.3)] was induced but without a focal activation pattern. One dog did not have inducible AF.

After posterior PV ostial ablation, AF was inducible in seven episodes from three dogs. The CL of AF increased to 156.0 ms (SD 10.3) ($P = 0.08$ vs. before posterior LSPV ostial ablation), whereas the duration of AF decreased to 10.2 s (SD 1.6) ($P < 0.001$ vs. before posterior LSPV ostial ablation). LOM focal activations were observed in four episodes from two dogs [CL 141.6 ms (SD 2.2); $P = $ not significant vs. before posterior ostial ablation]. However, no LSPV focal activations were observed in any dog after posterior LSPV ostial ablation (vs. 6 of 8 dogs before ablation; $P = 0.01$) (Fig. 6D).

LA-PV Conduction Breakthrough Via LOM After Segmental PV Ostial Ablation

Figure 7 illustrates LOM activation patterns in another dog during LAA pacing (200-ms CL), showing that conduction breakthrough into the LSPV can occur after segmental ostial ablation via LOM-LSPV connections. Figure 7, A–C, are before posterior LSPV ostial ablation, and Fig. 7, D–F, are after ablation. In each instance, isochronal maps of one beat are displayed (Fig. 7, A and D). Dynamic activation maps (Fig. 7, B and E) of the same beat as the isochronal maps are also displayed. In Fig. 7, A and D, a–i, indicates the location of the electrograms displayed. In Fig. 7A, LOM wave front was unable to connect to the LSPV because the LSPV had been activated <30 ms earlier and was therefore refractory [LSPV...
ERP 108.6 ms (SD 19.5). However, posterior ostial ablation resulted in conduction block into this LSPV, as illustrated most clearly by the 26-ms window in Fig. 7E. Thus the LOM wave front was now able to activate LSPV via direct LSPV-LOM connections, as the LSPV was nonrefractory. We observed this pattern in two dogs during SR or LAA pacing. These two dogs continued to have AF after ablation, with focal activations within LOM in four of five episodes but none within LSPV. During these episodes, LOM wave fronts were seen to bypass the LA-LSPV junction and exit within the LSPV. The presence of these additional LOM wave fronts was associated with persistently rapid LSPV activations [CL 151.8 ms (SD 4.8)] during AF in these two dogs even though the LSPV no longer demonstrated focal discharge. The relative contribution of LOM to LSPV activations during AF in these two LSPVs increased from 53.7% (SD 10.5) to 90.8% (6.1) after posterior ostial ablation (P = 0.09). The data indicate that the LOM may act as an accessory pathway that allows activation to break through into the LSPV despite RF ablation to electrically disconnect PV from LA.

**Histology**

Figure 8, A and C, is low-power views of longitudinal segments of the anterior and posterior LSPV-LA junctions, respectively, in the same dog. Figure 8B is a high-power (×20) view of box 1 in Fig. 8A, whereas Fig. 8D is a high-power view of box 2 in Fig. 8C. The posterior LSPV-LA junction (Fig. 8D) showed transmural changes such as myocyte hypereosinophilia (yellow arrow) and myocyte and epicardial connective tissue basophilia (green arrow). These changes are compatible with transmural, thermal ablation damage. On the other hand, the anterior LSPV-LA junction (Fig. 8B) was spared from these changes. In Fig. 8E, the MB within the LOM connects directly (yellow asterisk) with the LSPV just beyond the LSPV-LA junction (dashed line). This connection allowed electrical propagation from the CS to exit in the LSPV without involving the LA. However, in three of eight dogs, the MB ended blindly (black asterisk, Fig. 8F) without connecting directly with the LSPV.

**DISCUSSION**

**Main Findings**

The main findings of this study are as follows. 1) The LOM provides an accessory pathway that connects the CS to the LSPV, bypassing the LA-PV junction both during SR and during AF. Furthermore, focal discharges from the LOM may contribute to rapid LSPV activation during AF. 2) After segmental posterior ostial ablation, LA-PV coupling was sufficiently diminished to prevent reinduction of focal discharges within the LSPV. However, the accessory pathway formed by the LOM allowed LOM focal discharges to break through into the LSPV and maintain rapid LSPV activations during AF. These findings indicate that LOM-LSPV connections may contribute to rapid activations within the LSPV and potentially explain the frequent involvement of the LSPV as an arrhythmogenic focus during AF (5, 7).

**Electrical Connection Between LOM and LSPV**

We demonstrated that the LOM may connect directly with the LSPV bypassing the LA-PV junction. The potential for an electrical connection depends on the state of activation of the downstream target at the time a wave front approaches it. During SR and LAA pacing, there is a fixed sequence of LA followed by PV and then MB activation. The LOM wave front...
propagates from proximal to distal and reaches the target PV without activating it because of refractoriness. However, during AF, this chronology is less predictable, and, potentially, the LOM wave front may approach the PV after its recovery from inactivation. As a result, functional electrical connections may be manifested only during AF, as was the case for two of five dogs. During rapid LA activation, LA wave front frequently blocks at the LA-PV junction because of decremental conduction. As a result, LOM-PV wave front propagation helps maintain rapid rates of PV activation that may be necessary to initiate triggered activity. In this study, we demonstrated the presence of electrical connections between the LSPV and LOM in five of eight dogs. The LSPVs with LOM connections had a higher rate of activation during AF and a greater propensity to focal activations than those without.

**PV-LA Connection and Mechanisms of AF**

The importance of atrial input into PVs in generating focal discharge within PVs is unclear. Clinical ablation studies indicate that after electrical disconnection of PVs the PVs remain largely quiescent or demonstrate slow spontaneous activity only when disconnected from the LA (4). This indicates that the induction of rapid focal discharge within PVs depends on atrial input into PVs, which in turn depends on the presence of good electrical connections between the PV and the LA. In this study, we sought to determine the inducibility of PV focal discharge by rapid LA pacing after segmental ostial ablation. Our results indicate that PV focal discharge was not inducible when PV-LA connection was diminished by segmental ostial ablation. These data confirm the importance of atrial input as critical in generating focal discharge. It is conceivable that RF ablation works because the focal discharge sites in the PVs were directly targeted. However, in our study, we used a small-tipped ablation catheter to deliver RF at discrete sites in the posterior ostium and, under direct vision, specifically avoided ablating the anterior junction. Despite this we were still unable to induce focal firing from the anterior junction after ablation. These findings suggest that the PV-LA junction, by facilitating PV-LA electrical interaction, allows rapid activation of the PV from the LA, promoting the induction of focal activations within the PV. A dynamic interplay between PV and LA activity may increase the rate of activation in both chambers (11). The increased activation rate may in turn facilitate the induction of triggered activity (2). The posterior wall of the LSPV has muscle bundles that directly connect to the LA, whereas the anterior LA-LSPV connection is frequently discontinuous (6). In this study we showed that ablation of the posterior LA-LSPV junction alone sufficiently reduced the electrical interaction between the LSPV and the LA to prevent LSPV focal activation. However, LOM focal activations were still present in two dogs. The accessory pathway provided by the LOM allowed LOM focal discharge to maintain rapid rates of LSPV activation, despite reduced LA electrical input. However, LSPV activation rate via LOM, although fairly rapid (CL ~150 ms), was still insufficient to induce focal discharge within the LSPV without LA input. This suggests that both LSPV-LA and LSPV-LOM connections together rather than alone contribute to the generation of focal discharges within the PV.

**Clinical Implications**

Electrical isolation of PVs by catheter ablation can achieve a cure of AF. The study suggests that in some cases the LOM can act as an accessory pathway for conduction to break through into the LSPV, resulting in failure of electrical isolation. In turn, the electrical interaction between the LSPV and the LOM may serve to maintain rapid rates of activation that contribute to AF. It is conceivable that where persistent conduction into the LSPV is observed, catheter ablation targeting the LOM may achieve disconnection of the LSPV. Secondly, the LOM course directly intersects the line between the mitral isthmus and the left inferior (LI) PV, the latter being frequently used as an additional ablation target in addition to encircling PV ablations. It is possible that the LOM is ablated by this approach and contributes to clinical outcome (12).

**Limitations**

Although our data were limited to the LSPV-LA junction, we chose to concentrate on this region specifically to study the interactions with between the PV, the LA, and the LOM at this strategic intersection of the three structures. The LSPV is the most arrhythmogenic vein (5), a fact that may be due, among other factors, to its direct interactions with the LOM. Although we did not find functional LOM-LSPV connections in all dogs, five of eight dogs represent a significant proportion and suggests that in at least half of all LSPVs mapped the LOM may contribute significantly to rapid LSPV activations. The LOM also passes close to the LIPV-LA junction and may connect with the LIPV directly. However, we did not map the LIPV specifically. It is possible that activation within the LIPV may connect directly with the LSPV via the LOM independently of their connections with the LA. Therefore, rather than LOM focal discharge activating the LSPV, the LOM may also act as a passive interventricular conduit for reciprocal activation of left-sided PVs (13). However, in this study, we specifically observed multiple activations from the LOM that are consistent with focal discharge. We did not ablate the LOM because the LOM may act as an accessory pathway for conduction to break through into the LSPV, resulting in failure of electrical isolation of the PV. The study suggests that in some cases the LOM can act as an accessory pathway for conduction to break through into the LSPV, resulting in failure of electrical isolation. In turn, the electrical interaction between the LSPV and the LOM may serve to maintain rapid rates of activation that contribute to AF. It is conceivable that where persistent conduction into the LSPV is observed, catheter ablation targeting the LOM may achieve disconnection of the LSPV. Secondly, the LOM course directly intersects the line between the mitral isthmus and the left inferior (LI) PV, the latter being frequently used as an additional ablation target in addition to encircling PV ablations. It is possible that the LOM is ablated by this approach and contributes to clinical outcome (12).

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**REFERENCES**


