High take-off left inferior pulmonary vein as an obstacle in creating a conduction block at the lateral mitral isthmus

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Aims
Creation of complete linear lesions in the lateral mitral isthmus (LMI) by catheter ablation for treating atrial fibrillation remains technically challenging. We aimed to clarify whether a high take-off left inferior pulmonary vein (LIPV) can hamper the creation of a complete block at the LMI.

Methods and results
We included 81 consecutive patients who underwent linear ablation at LMI and cardiac computed tomography (CT) before ablation. We defined a high take-off LIPV when the level of the lower edge of the LIPV ostium was higher than that of the top of mitral annulus on CT. The clinical backgrounds, parameters, and long-term follow-up were then compared between the success (successful creation of a complete LMI block) and failure groups. A complete LMI block was obtained in 60/81 (76%) patients. In the failure group, a high take-off LIPV was noted more commonly and the LMI tended to be longer than the success group. Multivariate analysis revealed that a high take-off LIPV was an independent predictor of failure to achieve a complete LMI block. The sinus rhythm maintenance rate was not different between the success and failure groups.

Conclusion
A high take-off LIPV hampered the creation of complete linear lesions in the LMI.

Keywords
Atrial fibrillation • Catheter ablation • Pulmonary vein • Computed tomography • Mitral isthmus

Introduction
The curative approach to atrial fibrillation (AF) by radiofrequency (RF) catheter ablation began with the targeting of the focus of the atrial extrasystole that triggered AF, mainly the foci originating from the pulmonary veins (PVs),1 and this approach was developed further into electrical PV disconnection.2,3 Recently, left atrial compartmentalization by catheter ablation has been deployed to improve sinus rhythm maintenance rate after PV disconnection.4,5 Although the lateral mitral isthmus (LMI)—lying between the left inferior PV (LIPV) and the mitral annulus (MA)—is one of the crucial targets for this procedure, the creation of complete linear lesions in LMI by catheter ablation is technically challenging.6 The factors responsible for these challenges remain to be investigated. Hence, in this study, we sought to clarify the predictors of failure to achieve a complete block in the LMI with emphasis on the anatomical relationship between the LIPV and the MA as defined by cardiac computed tomography (CT).

Methods
Study population
In this study, we included 81 consecutive patients (70 males; mean age: 53 ± 10 years) who underwent linear ablation at LMI in Lariboisie`re University Hospital. This group consisted of 28 patients with persistent or permanent AF and 53 of paroxysmal AF. Of the latter group, 26 patients had recurrent AF after PV disconnection, 14 had persistent AF after PV disconnection, and 13 had longer AF episodes (>24 h). This procedure was the first ablation targeting AF for 42 patients and the second procedure for 31 patients and the third procedure.

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High take-off LIPV as an obstacle in creating conduction block at LMI

Table 1  The baseline characteristics of the patients in the success and failure groups

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Success</th>
<th>Failure</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>81</td>
<td>61</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>53 ± 10</td>
<td>53 ± 10</td>
<td>54 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>70 (86%)</td>
<td>53 (87%)</td>
<td>17 (85%)</td>
<td>NS</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>53 (65%)</td>
<td>49 (64%)</td>
<td>14 (70%)</td>
<td>NS</td>
</tr>
<tr>
<td>History of AF (years)</td>
<td>8.9 ± 6.5</td>
<td>8.7 ± 6.2</td>
<td>9.6 ± 7.2</td>
<td>NS</td>
</tr>
<tr>
<td>AAD</td>
<td>3.5 ± 1.2</td>
<td>3.6 ± 1.3</td>
<td>3.2 ± 1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>75 (93%)</td>
<td>56 (92%)</td>
<td>19 (95%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>27 (33%)</td>
<td>20 (33%)</td>
<td>7 (35%)</td>
<td>NS</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>43 ± 6</td>
<td>44 ± 6</td>
<td>42 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>LA area (cm²)</td>
<td>24 ± 7</td>
<td>24 ± 7</td>
<td>23 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>60 ± 11</td>
<td>60 ± 10</td>
<td>61 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>LV end-diastolic diameter (mm)</td>
<td>53 ± 6</td>
<td>53 ± 6</td>
<td>52 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>LV end-systolic diameter (mm)</td>
<td>35 ± 7</td>
<td>36 ± 7</td>
<td>34 ± 9</td>
<td>NS</td>
</tr>
</tbody>
</table>

Cardiac disease: HCM, 4; DCM, 12; CAD, 6; valvular heart disease, 5; P-value: success vs. failure.

for 8 patients and the first procedure targeting LMI for all patients. The baseline characteristics of these patients are shown in Table 1. All patients underwent echocardiography and cardiac CT before catheter ablation.

Electrophysiological study and catheter ablation

After obtaining written informed consent, single-plane fluoroscopy-guided ablation was performed using an irrigated-tip catheter (Celsius Thermocool, D curve; Biosense Webster, Diamond Bar, CA, USA) at an irrigation rate of 15–40 mL/min. Intravenous heparin was administered routinely and titrated every 30 min during left atrial catheterization (target-activated clotting time, ~250–350 s). A diagnostic 6 F decapolar catheter (Response; St Jude Medical, Minnetonka, MN, USA) was introduced into the coronary sinus (CS) for electrical stimulation and intracardiac electrography. All patients underwent PV disconnection guided by a circular mapping catheter (Lasso variable; 25–15 mm; Biosense Webster) based on a previously described procedure. The aim was to achieve complete elimination of PV electrical activity by delivering an RF current (maximum RF power, 30 W) proximally to each PV ostium. After PV disconnection, linear ablation at the LMI was performed as described by Jais et al. A continuous RF current was delivered along the region from the MA to the LIPV (maximum RF power, 45 W). The ablation catheter was dragged upon the reduction of the local atrial potentials. Catheter contact was facilitated by a long sheath (Preface; Biosense Webster). After the first passage, we dragged the ablation catheter on the pre-sumed ablation line and delivered additional RF pulses at points where atrial potentials were still present. In cases where endocardial ablation was unable to successfully achieve a complete conduction block in the LMI, further RF pulses (maximum power, 25 W) were delivered within the distal CS.

If needed, some patients also underwent linear ablation at the left atrial roof between the left and right superior PVs by a method described by Hocini et al. and/or linear ablation at the cavo-tricuspid isthmus.

Complete bidirectional LMI block was confirmed using the criteria reported previously, which included the presence of widely separated local double potentials along the length of the ablation line during CS pacing septal of the line and mapping the activation detour during pacing from either side of the line. We compared the clinical data and the CT parameters described below between patients who underwent successful linear ablation at LMI (success group) vs. those who did not (failure group).

Computed tomography imaging

Before catheter ablation, cardiac CTs were obtained using a multidetector-row spiral CT scanner (Somatom Plus 4 Volume Zoom WIP-version VA 20; Siemens, Forchheim, Germany, or GE Lightspeed 16; General Electrical Medical Systems, Milwaukee, WI, USA). All patients provided informed consent. Image acquisition was performed during an inspiratory breath-hold. Imaging was initiated at the transaxial level of the aortic arch and carried caudally to cover the cardiac chambers. Non-ionic iodinated contrast material (Omnipaque 300) was administered intravenously (100–120 mL at 2.5–3.0 mL/s) before and during scanning.

Computed tomography parameters

Image data were reconstructed with a DICOM viewer capable of constructing a three-dimensional (3D) image (DIAM Viewer; Global Imaging Online, Paris, France). We created an oblique sagittal plane spanning the lower edge of the LIPV ostium and the top of the MA to measure the difference between the levels of these structures—the LIPV – MA difference. If the lower edge of the LIPV ostium was higher than the top of the MA, the LIPV – MA difference was positive; this was defined as a high take-off LIPV (Figure 1). We then created an oblique axial plane including the LIPV and MA to determine the minimal distance between them, representing the length of the LMI (Figure 2) and also measured the endocardial LMI length. The left PVs were defined to have a common ostium when the bifurcation was located 5 mm distal to the anterior ridge between the left PVs and the left atrial appendage (LAA).

Cardiac echo parameters

The antero-posterior LA diameter, LA area, left ventricular ejection fraction, left ventricular diastolic diameter, and left ventricular systolic...
diameter were measured and compared between the success and failure groups.

**Patient follow-up**

Patients underwent Holter monitoring immediately after catheter ablation and were continuously monitored for 5 days. They were then followed up every 3 months with surface electrograms and Holter monitoring at the outpatient clinic of our hospital or of the referring physicians. Additional surface electrograms and Holter monitoring were carried out in patients having arrhythmic symptoms. The sinus rhythm maintenance rate after ablation was compared between the success and failure groups.

**Statistical analysis**

Data were expressed as the average ± SD. Relevant variables between the success and failure groups were compared by the Student’s t-test for numerical data, χ² analysis for categorical data, and multivariate analysis using a logistic regression model. The correlation between the left atrial diameter and area and the length of the LMI and the LIPV – MA difference was examined by the Pearson product-moment correlation coefficient. The sinus rhythm maintenance rate after catheter ablation was compared between the success and failure groups by Kaplan–Meier curves and examined by the log-rank test. In all cases, a value of $P < 0.05$ was considered as significant. Statistical analysis was performed using the StatView software (SAS Institute Inc., Cary, NC, USA).

**Results**

**Catheter ablation**

Pulmonary vein disconnection was obtained in 100% patients, and ablation from within the CS was performed in 73/81 (91%) patients while attempting to create complete linear LMI lesions. Totally, 29 ± 14 RF pulses (mean power, 32 ± 5 W; total ablation time, 1551 ± 800 s) were delivered to the LMI [endocardial ablation: 23 ± 12 RF pulses (power, 34 ± 5 W; ablation time, 1307 ± 643 s) and ablation from within the CS: 6 ± 5 RF pulses (power, 20 ± 4 W; ablation time, 222 ± 183 s)]. A complete bidirectional LMI block was successfully created in 61 patients, resulting the single procedure success rate of 76%.
The number of RF pulses and total ablation time in the failure group (32 ± 14 and 1729 ± 928 s, respectively) tended to be higher than those in the success group (27 ± 14 and 1463 ± 728 s, respectively); however, the difference was not statistically significant. Also, the temperature, the power, and the impedance were not different comparing both groups (failure vs. success group: 40 ± 1 vs. 40 ± 1, 31 ± 2 vs. 32 ± 5, and 98 ± 24 vs. 99 ± 23). External shock was needed in 20 patients in whom ablation did not terminate AF, and complete LMI block was validated after sinus rhythm resumed. In 61 patients with a complete conduction block in the LMI, the mean conduction time from the stimulus to the LAA obtained by distal CS electrode pacing was 151 ± 40 ms and that from the stimulus to distal CS electrodes obtained by LAA pacing was 153 ± 36 ms. Linear ablation was applied on the left atrial roof line in 63 patients and on the cavo-tricuspid isthmus in 66 patients.

In one patient, the procedure was complicated by cardiac tamponade, which was treated by percutaneous drainage. During epicardial ablation at the LMI, one patient developed acute occlusion in the middle part of the left circumflex coronary artery, which was immediately treated with successful percutaneous catheter intervention.

**Success group vs. failure group**

**Baseline characteristics**
The baseline characteristics of the patients in the success and failure groups (Table 1) did not differ significantly. And also there were no significant differences with regard to the number of patients who underwent an additional linear ablation at the left atrial roof line [75 vs. 85%, respectively (P = NS)] and at the cavo-tricuspid isthmus [82 vs. 80%, respectively (P = NS)].

**Cardiac computed tomography parameters**
The cardiac CT parameters are summarized in Table 2. A left common ostium was observed in 50/81 (62%) patients, and there was no significant difference in the distribution of these cases between the success and failure groups. The mean LMI length was 29.4 ± 7.1 mm (range, 17.3–60.7 mm), which tended to be greater in the failure group than in the success group (32.0 ± 9.0 and 28.5 ± 6.2 mm, respectively; P = 0.06) and the mean endocardial LMI length was 33.5 ± 8.9 mm (range, 18.2–69.1 mm), which tended to be greater in the failure group than in the success group (36.5 ± 10.4 and 32.4 ± 8.1 mm, respectively; P = 0.09). The mean LIPV – MA difference was –3.9 ± 9.3 mm (range, −23.7 to 19.1 mm), indicating that the lower edge of the LIPV ostium was situated 3.9 mm lower (more caudally) than the top of the MA in all patients. Characteristically, the mean LIPV – MA difference was −5.7 ± 7.7 and 1.3 ± 11.6 mm in the success and failure groups, respectively (P = 0.006), indicating that the LIPV ostium was positioned higher (more cranially) in the failure group than in the success group. A high take-off LIPV, defined as an LIPV – MA difference >0, was observed in 26/81 (32%) patients: 13 (21%) in the success group and 13 (65%) in the failure group (P = 0.0006). LMI length of patients with high
take-off LIPV and non-high take-off LIPV was 30.9 ± 8.0 and 28.9 ± 7.9 mm (P = NS), respectively. Among these patients, a complete LMI block was created in 13 (50%) patients; in the remaining 55 patients who did not have a high take-off LIPV, a complete LMI block was created in 48 (87%) patients. Both the LMI length and the LIPV – MA difference showed normal distribution (P < 0.0001 in both cases), and these parameters did not show a significant positive correlation (R^2 = 0.03, P = 0.13).

The relationships between the results of linear ablation, the LMI length, and the LIPV – MA difference are shown in Figure 3. The LMI length showed a weak positive correlation with the LA diameter on echocardiography (LMI length = 5.374 + 0.557 × LA diameter, R^2 = 0.198, P < 0.0001), whereas the LIPV – MA difference did not correlate with the LA diameter. Logistic regression showed a high take-off LIPV as an independent predictor of failure to achieve a complete LMI block (odds ratio, 5.7; 95% confidence intervals: 1.8–17.7; P = 0.003), whereas the LMI length was not an independent predictor (odds ratio, 1.1; 95% confidence intervals: 0.99–1.16; P = 0.10).

**Long-term outcome**

The average follow-up period was 448 ± 29 days (449 ± 33 and 437 ± 58 days in the success and failure groups, respectively). The arrhythmia-free survival curves of the success and failure groups showed no significant difference with regard to maintenance of sinus rhythm (64 ± 7% vs. 59 ± 13%, in the success and failure groups, respectively; P = NS).

**Discussion**

**Main findings**

We successfully demonstrated the variations in the craniocaudal anatomical relationship between the LIPV and the MA, and the high take-off LIPV was associated with unsuccessful linear ablation at the LMI and an independent predictor of failure of linear ablation at the LMI.

**Anatomy and histology of the lateral mitral isthmus**

The anatomical and histological aspects of the difficulties in achieving a complete linear LMI block have been speculated. Becker^8^ reported that the myocardial thickness along the LMI was as follows: 3 mm near the PV, 2.8 mm in the middle portion, and 1.2 mm near the MA, and the LMI length was 34.6 mm in 20 post-mortem hearts. Wittkampf et al.^9^ also reported that the mean thickness was revealed to be 3.8 ± 0.9 mm and the length to be 35.7 ± 7 mm in 16 post-mortem hearts. The LMI was reported to be 1.5 times longer than the cavotricuspid isthmus; however, there was no difference between the myocardial thickness along them.10

Epicardial coronary vessels have been reported to be possible obstacles in creating a transmural lesion by RF ablation both experimentally and clinically,11,12 indicating that these structures could have some cooling effects. The CS and the left circumflex artery, which courses along the epicardial side of the LMI, might play some role. The myocardial sleeve around the CS is considered to hamper the creation of complete linear lesions, since it may be difficult to apply RF from the endocardium in order to ablate the epicardial wall of the myocardial sleeve. According to Wittkampf et al.,9 a connecting myocardial sleeve at the LMI

**Table 2**

<table>
<thead>
<tr>
<th>Cardiac CT parameters</th>
<th>Overall</th>
<th>Success</th>
<th>Failure</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left common ostium</td>
<td>51 (63%)</td>
<td>37 (61%)</td>
<td>14 (70%)</td>
<td>NS</td>
</tr>
<tr>
<td>Length of LMI (mm)</td>
<td>29.4 ± 7.1</td>
<td>28.5 ± 6.2</td>
<td>32.0 ± 9.0</td>
<td>0.06</td>
</tr>
<tr>
<td>LIPV – MA difference (mm)</td>
<td>–3.9 ± 9.3</td>
<td>–5.7 ± 7.8</td>
<td>1.3 ± 11.6</td>
<td>0.004</td>
</tr>
<tr>
<td>High take-off LIPV</td>
<td>26 (32%)</td>
<td>13 (21%)</td>
<td>13 (65%)</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

LIPV, left inferior pulmonary vein; MA, mitral annulus; high take-off PV, LIPV – MA difference ≥ 0 mm.

**Figure 3**

Relationship between the result of linear ablation at the LMI, the LMI length, and the LIPV – MA difference. LIPV – MA difference was significantly longer in failure group than success group shown in a box and whiskers plot. Abbreviations are the same as in Figure 1.
level was present in only 1/16 specimens. In such cases, complete ablation around the myocardial sleeve or complete isolation of the myocardial sleeve would be needed.

Chiang et al. reported three types of LMI morphology on 3D CT, namely concave, straight, and pouch-like, which could affect the result of linear ablation at the LMI.14 These morphological variations were also reported in the cavo-tricuspid isthmus and could influence the results of linear ablation at the cavo-tricuspid isthmus.14–16

High take-off left inferior pulmonary vein None of the literatures have referred to the anatomical relationship between the LIPV and the MA; however, there were considerable variations in the position of the LIPV ostium opening into the LA, assessed in a craniocaudal direction. A maximum LIPV – MA difference of ~4 cm was noted among the patients included in this study, standardized according to the level of the top of the MA.

This study showed that the success rate of achieving a complete LMI block was 50% in patients with a high take-off LIPV, whereas in patients who did not have a high take-off LIPV, it was 87%. Technically, linear ablation at the cavo-tricuspid isthmus can be performed by simply dragging the ablation catheter back from the tricuspid annulus, since the direction of the ablation line is parallel to that of the catheter. However, for performing linear ablation at the LMI, the catheter needs to be moved from the MA to the LIPV in a direction perpendicular to that of the catheter while applying a clockwise torque on it and bending it caudally. Moreover, the imaginary line on the LMI along which ablation is performed is supposed to course obliquely in patients with a high take-off LIPV. In such cases, catheter manipulation to make complete linear lesions is considered to be even more complicated and considered to be difficult.

We measured the difference in the height of the lower edge of the LIPV ostium and that of the top of the MA to determine cases having a high take-off LIPV. However, a simpler method to possibly judge patients without a high take-off LIPV would be to observe the LIPV and the left ventricular cavity on the same axial cardiac CT, as shown in Figure 1.

We could not find positive correlation between the length of LMI and the LIPV – MA difference. This might be caused by some patients who had a long antero-posterior diameter of the left atrium who did not have high take-off PV.

Limitations In this study, the result of linear ablation at LMI was achieved by using an ablation catheter under single-plane fluoroscopic guidance. Our analysis was valid only for the type of catheter and the type of energy we used. It remains unclear whether a non-fluoroscopic mapping system could have led to more favorable results in achieving the complete LMI block. Some papers reported the effectiveness of the non-fluoroscopic mapping system.5,17,18 The number of patients included in these studies was limited, and the potential role of the non-fluoroscopic mapping system for use in linear ablation at the LMI remains to be elucidated.

The anatomical relationship on CT might not be reproducible during the ablation procedure because the respiratory phase differs. However, we believe that the anatomical characteristics on CT reflect the individual anatomical characteristics of the patients because the conditions of CT scanning were consistent.

The long-term outcome of the success group was not better than that of the failure group. However, several factors could affect the long-term outcome, most importantly the small number of patients comprising the failure group.

Finally, we did not perform analysis of the myocardial thickness, diameter of the CS, left atrial volume measured by CT, local CS electrograms, and the pouch-like morphology at the LMI, which are the limitations of this study.

Conclusion In patients with a high take-off LIPV, it is difficult to achieve a complete conduction block in the LMI by single-plane fluoroscopy-guided ablation using an irrigated-tip catheter.

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Conflict of interest: none declared.

References

Pulmonary vein stents or stenosis: why acquisition phase matters during computed tomography?

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A 26-year-old female who had pulmonary vein (PV) stenting for PV stenosis in two out of four PVs following PV ostial isolation presented with acute dyspnoea and chest pain. Computed tomography (CT) per pulmonary embolism (PE) protocol suggested PV in-stent stenosis on therapeutic warfarin (Figure 1A). Repeat cardiac CT using left atrium (LA)/PV protocol within 12 h revealed patent stents averting inadvertent cardiac intervention (Figure 1B). Patient’s symptoms were thought to be from recurrent atypical atrial flutter. Due to acquisition phase differences, PE protocol does not allow clear evaluation of PVs. Cardiac CTs with the LA/PV protocol provide assessment of PVs.

Figure 1 Cardiac CT image of PVs with PE and LA/PV protocols.

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