Local Coronary Flow Is Associated With an Unsuccessful Complete Block Line at the Mitral Isthmus in Patients With Atrial Fibrillation

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Background—The addition of a mitral isthmus (MI) block line after pulmonary vein isolation could lead to a favorable outcome of catheter ablation in patients with atrial fibrillation (AF). However, it is sometimes tough to create a complete MI block line, and the cooling effect because of the local coronary flow may prevent the creation of a successful MI block line.

Methods and Results—This study enrolled 81 AF patients in whom the creation of an MI block line was attempted in those with persistent or pacing-inducible AF after pulmonary vein isolation. A local coronary artery (LCA) across the MI block line was observed in 43 (53%) of 81 patients, and a bidirectional MI block was successfully accomplished in 53 (65%) of 81 patients, at the estimated MI line. The ratio of a successful MI block line was significantly lower in the patients with an LCA than in those without an LCA (42% versus 92%; P<0.001). The mean diameter of the coronary sinus (0.59±0.18 versus 0.82±0.22 cm; P<0.001) and length of the estimated MI line (33.4±9.9 versus 29.4±7.1 mm; P=0.032) were significantly shorter in the patients with a successful MI block line than in those without a successful MI block line. In the multivariable analysis, an LCA at the MI and a larger coronary sinus diameter were independent risk factors for an unsuccessful MI block line.

Conclusions—Local coronary flow at the MI is associated with an increased incidence of an unsuccessful MI block line.

Key Words: ablation ■ atrial fibrillation ■ circulation ■ electrophysiology mapping

A additional ablation (atrial fibrillation [AF]) of the mitral isthmus (MI), lying between the left inferior pulmonary vein (PV) and mitral annulus, after PV isolation could improve the outcome of AF. However, the creation of a complete electric block line is still technically challenging and time-consuming,1 and an incomplete interruption with slow residual conduction may be proarrhythmic and may increase the incidence of gap-related re-entrant atrial tachyarrhythmias.2,3

To the best of our knowledge, there have been no previous reports concerning the relationship between the local coronary flow (LCF), including the LCA, CS, and conduction block at the MI. In this study, we evaluated the relationship between the LCF and the creation of a successful electric MI block line.

Methods

Study Population
The study population consisted of 81 consecutive patients who underwent RF ablation. The patients’ mean age was 66 years, 60 (74.1%) were male, and 42 (52.0%) had persistent AF lasting >7 days. The mean AF duration was 36.3 months. The exclusion criteria were as follows: (1) a left atrial (LA) diameter >55 mm, (2) significant valvular disease requiring surgery, (3) an ejection fraction <40%, (4) hypertrophic obstructive cardiomyopathy, and (5) long-lasting AF (>10 years). All antiarrhythmic agents were generally discontinued for at least 3 days before the CA. All patients provided their written informed consent for the electrophysiological study and ablation procedure. This study was approved by our institutional review committee, and the subjects gave their informed consent.
Coronary and PV Angiography

Just before the ablation procedure, cine angiography was performed with a spontaneous contrast medium injection from long sheaths located in the upper and lower left PVs, and the location of the PV ostia was determined. Afterwards, coronary angiography was performed to evaluate the LCA at the MI lesion using the left and right anterior oblique projections (Figure 1 and Figure 2). The course of the CS was determined by a subsequent filling and staining with contrast and/or by noting the location of the multipolar electrodes of the catheter within the CS (Figure 3).

The diameters of the LCA and CS were determined in the left anterior oblique 45° view and measured by the quantitative coronary analysis method (Figure 3). The estimated length of the MI line was determined as the distance between the lower margin of the left inferior PV ostium and mitral valve, as observed in the PV angiography image.

Electrophysiological Study and CA

Transesophageal echocardiography was performed to exclude any LA thrombi. A 20-pole diagnostic catheter was positioned in the CS for pacing and recording. The 20-pole catheter was located in the right atrium to cover the area of the tricuspid annulus or superior vena cava. The LA and PVs were accessed by a transseptal approach.

We introduced 3 steerable catheters, including 2 spiral curve catheters, into the left atrium through a single transseptal puncture site. The PVs were mapped with a circumferential 10- or 20-pole catheter (IBI; Irvine, CA). The surface ECG and intracardiac electrograms filtered at 30 to 500 Hz were recorded simultaneously with a polygraph (DUO EP Laboratory; Bard Electrophysiology; Lowell, MA). A single bolus of 150 IU/kg of heparin was administered after the transseptal puncture and repeated to maintain an activated clotting time of >300 s.

The electroanatomical geometry of the LA chamber was created (Ensite NavX; St Jude Medical). We initially performed the PV isolation procedure using a double circular mapping catheter technique. The RF energy was principally applied during the sinus rhythm. In the patients with AF persistence, direct cardioversion was initially attempted to restore sinus rhythm. The RF energy was circumferentially applied to isolate the PV potentials, and we confirmed the success of an individual electric PV isolation by monitoring the electric isolation at the antrum level (>1 cm from the ostium of both the right and left PVs). The complete disappearance of the potentials from all 4 PVs and the antrum area inside the created line were confirmed in all patients. A left PV isolation was initially accomplished, followed by a right PV isolation.

After the PV isolation procedure, atrial tachyarrhythmias were immediately induced by intense burst pacing. Atrial burst pacing was performed (10-s bursts) in decrements from 250 ms down to refractoriness at the maximum output or 150 ms from at least 3 sites.
including the distal CS, the LA appendage, and the right atrium. Inducible AF was defined as AF that was sustained for ≥1 minute. When the AF spontaneously terminated, induction was attempted 3 times from each of these sites. In cases with induction of burst-inducible AF after the PV isolation procedure, additional roof and MI lines were created.

The local bipolar electrograms at the MI were recorded using a 20-pole diagnostic catheter with 2-mm interelectrode spacing positioned in the CS just before the CA. We measured the local electrogram at a site that was consistent with the location of the MI line (Figure 4). At the commencement of the MI ablation, a spiral catheter was placed in the LA appendage and constant pacing was delivered from the LA appendage base if the patient was in sinus rhythm. A complete bidirectional MI block was confirmed by the presence of widely separated local double potentials along the length of the ablation line during CS pacing septal to the line and mapping the activation detour during pacing from either side of the line. If a conduction block was not achieved, then ablation was performed within the distal CS at a point approximating the annular end of the endocardial line.

RF energy was delivered for 30 to 45 s at each site using an 8-mm-tip dumbbell-shaped catheter (Japan Life Line Co, Ltd; Tokyo, Japan). The RF energy was delivered with a power of 35 W toward the PVs and 40 W toward the roof and MI line. In cases in which a complete block line could not be obtained at these energy levels, RF energy was increased up to 45 W. The temperature was limited to 55°C. Within the CS, ablation was delivered at 25 W. Ablation within the CS was continued for up to 5 minutes or until the conduction block was not achieved, then ablation was performed within the distal CS at a point approximating the annular end of the endocardial line.

**Statistical Analysis**
Continuous variables are expressed as mean±SD. The variables were compared by a 2-sample t test or a χ² test. Data without a normal distribution were expressed as the median (25th–75th percentile) and compared by a Mann-Whitney U test that was used for the nonparametric analysis. A logistic regression analysis was used to assess the relationship between the predictive variables and a successful MI block, and then the significant factors related to a successful MI block (P<0.1) from the univariable analysis were incorporated into the multivariable model. Wald backward selection was used to detect the significant independent factors related to a successful MI block line. Receiver operating characteristic curve analyses were used to determine the optimal cutoff values of CS diameter that provide the best sensitivity and specificity for a successful MI block line. All analyses were performed using SPSS 10.0 statistical software (SPSS Inc; Chicago, Ill).

**Results**

**Relationship Between the Coronary Angiogram and MI**
An LCA across the MI was observed in 43 (53%) of 81 patients. The angiographic findings in the cases with and without an LCA are described in Figure 1. The LCA originated from the left coronary artery in 39 (91%) of 43 patients and from the number 4 AV branch in 4 (9%) of 43 patients. The distance from the lower margin of the CS to the mitral isthmus (MI) block line between the patients with and without a successful MI block line (57% versus 82%; P<0.001) (Figure 5). The need for subsequent RF from inside the CS was significantly less in the patients with a successful MI block line than in those without a successful MI block line (57% versus 82%; P=0.026). In the patients with a successful MI block line, the need for additional epicardial ablation from the CS was significantly higher in the cases with an LCA than in those without an LCA (27% versus 86%; P<0.001). We could not successfully insert the ablation catheter into the CS because of the sharp curved...
Table 1. Clinical Factors and Structural Parameters Associated With a Successful MI Block Line

<table>
<thead>
<tr>
<th>Variables</th>
<th>Positive (n=53)</th>
<th>Negative (n=28)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical factors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age, y</td>
<td>63.0±10</td>
<td>67.8±8.0</td>
<td>0.036</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>70</td>
<td>82</td>
<td>0.24</td>
</tr>
<tr>
<td>Persistent AF, %</td>
<td>48</td>
<td>56</td>
<td>0.53</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>51</td>
<td>77</td>
<td>0.039</td>
</tr>
<tr>
<td>SHD, %</td>
<td>24</td>
<td>33</td>
<td>0.45</td>
</tr>
<tr>
<td>AF duration, mo</td>
<td>40 (18–86)</td>
<td>36 (16–92)</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>Structural parameters</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>LAD, mm (A-P)</td>
<td>38.5±8.3</td>
<td>39.5±6.6</td>
<td>0.43</td>
</tr>
<tr>
<td>S-L</td>
<td>40.7±6.3</td>
<td>39.5±6.6</td>
<td>0.44</td>
</tr>
<tr>
<td>MV-PV</td>
<td>55.4±7.6</td>
<td>55.6±7.9</td>
<td>0.90</td>
</tr>
<tr>
<td>LA volume, cm³</td>
<td>67.1±20.3</td>
<td>70.6±29.4</td>
<td>0.61</td>
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<tr>
<td>PV diameter, mm</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Left upper PV</td>
<td>20.2±4.1</td>
<td>19.6±3.6</td>
<td>0.62</td>
</tr>
<tr>
<td>Left lower PV</td>
<td>15.0±2.6</td>
<td>16.0±2.6</td>
<td>0.20</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>64.7±7.3</td>
<td>61.4±7.2</td>
<td>0.14</td>
</tr>
</tbody>
</table>

A-P indicates anterior-posterior; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; MV-PV, mitral valve–pulmonary vein roof; s-MI, successful MI; SHD, structural heart disease; S-L, septal-lateral.

angle of the CS ostium and/or CS valve in 4 (18%) of 27 patients without a successful MI block line. Cardiac tamponade occurred in 1 (1.2%) of 82 patients during the ablation in those cases requiring epicardial ablation, and nonsurgical drainage was successfully performed in those cases.

Factors Associated With a Successful MI Block Line

An MI block was successfully accomplished in 53 (65%) of 81 patients. The procedure time was significantly longer in the patients with a successful MI block line than in those without a successful MI block line (median, 18.9 versus 8.3 minutes; \( P<0.001 \)). The relationship between the clinical and structural factors associated with and without a successful MI block line is shown in Table 2. The age (63.0±10 versus 67.8±8.0 years; \( P=0.036 \)) and hypertension (51% versus 77%; \( P=0.039 \)) were significantly lower in the patients with a successful MI block line than in those without a successful MI block line. The LA diameter, LA volume, left PV diameter, and left ventricular function had no significant association with achieving a successful MI block line.

The relationship of the local angiographic and electrophysiological findings at the MI in those with and without a successful MI block line is shown in Table 2. The incidence of an LCA across the MI line was significantly lower in the patients with a successful MI block line than in those without a successful MI block line (34% versus 89%; \( P<0.001 \)). The mean diameter of the CS (0.59±0.18 versus 0.82±0.22 cm; \( P<0.001 \)) was significantly smaller, and the length of the estimated MI line (33.4±9.9 versus 29.4±7.1 mm; \( P=0.032 \)) was significantly shorter, in the patients with a successful MI block line than in those without a successful MI block line. The atrial wave amplitude was significantly lower in the patients with a successful MI block line than in those without a successful MI block line.

The results of univariable and multivariable analyses for successful MI block were demonstrated in Table 3. The results of the multivariable analysis revealed that the mean CS diameter (0.005 [0.00–0.18]; \( P=0.001 \)) and an LCA across the MI (0.16 [0.04–0.62]; \( P=0.008 \)) were the independent risk factors for a successful MI block line. The optimal cutoff of the CS diameter at the MI was 6.7 mm, according to receiver operating characteristic curve analysis, and the sensitivity and specificity values

Table 2. The Local Angiographic and ECG Characteristics of an MI Associated With a Successful MI Block Line

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Positive (n=53)</th>
<th>Negative (n=28)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angiographic findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCA at the MI, %</td>
<td>34</td>
<td>89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diameter of the LCA at the MI, mm</td>
<td>1.9±0.7</td>
<td>2.2±1.0</td>
<td>0.35</td>
</tr>
<tr>
<td>Diameter of the CS at the MI, mm</td>
<td>5.9±1.8</td>
<td>8.2±2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of the MI line, mm</td>
<td>29.4±7.1</td>
<td>33.4±9.9</td>
<td>0.032</td>
</tr>
<tr>
<td><strong>ECG findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V-wave amplitude, mV</td>
<td>0.30 (0.12–0.77)</td>
<td>0.34 (0.14–0.66)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

N indicates negative; P, positive; s-MI, successful MI.

Table 3. The Results of the Multivariable Analysis of a Successful MI Block Line

<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCA at the MI (yes or no)</td>
<td>0.06 (0.02–0.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diameter of the CS (measured in mm)</td>
<td>0.009 (0.00–0.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of the MI line (measured in mm)</td>
<td>0.64 (0.37–0.94)</td>
<td>0.032</td>
</tr>
<tr>
<td>A amplitude (measured in mV)</td>
<td>0.57 (0.31–0.97)</td>
<td>0.042</td>
</tr>
<tr>
<td>Age (measured in years)</td>
<td>0.96 (0.92–0.99)</td>
<td>0.036</td>
</tr>
<tr>
<td>Hypertension (yes or no)</td>
<td>0.27 (0.08–0.93)</td>
<td>0.039</td>
</tr>
</tbody>
</table>

Odds Ratio (95% CI)
for an unsuccessful MI block were 78% and 68%, respectively (area under the curve, 0.76±0.05). The sensitivity and specificity values of an LCA across the MI for an unsuccessful MI block were 89% and 66%, respectively (area under the curve, 0.78±0.05).

Discussion
In this study, an LCA across the MI was observed in approximately half of the enrolled AF patients. The ratio of successful MI block lines was significantly lower in the patients with an LCA than in those without an LCA. The mean diameter of the CS was significantly smaller in the patients with a successful MI block line than in those without a successful MI block line. In the multiple variable analyses, an LCA across the MI and a larger CS diameter were significant independent related factors for an unsuccessful MI block line. These findings demonstrated that the presence of an LCA could promote difficulties in accomplishing the creation of a complete block line at the MI.

Clinical Implications of an MI Block Line
The complete electric block of the MI after PV isolation is the crucial target to improve the outcome of the RF ablation procedure, especially in patients with advanced remodeled atria or AF persistency. However, RF CA to create an MI block is sometimes technically difficult, and additional RF applications within the CS are often required to accomplish the creation of a complete MI block line with an increase in the risk of complications, such as a pericardial tamponade, CS stenosis, and possible esophageal damage. On the other hand, an incomplete line has a high likelihood of the occurrence of gap-related mitral re-entrant tachyarrhythmia.9–11

Local Coronary Flow and Transmural Block at the MI
In this study, an LCA across the MI could be observed in approximately half of the enrolled AF patients, which seemed to protect them from any transmural linear damage during the RF application in that area. An LCA across the vicinity of the RF lesion, even if from small vessels, might reduce the lesion size and preserve the conduction through the linear RF lesion, because the cooling effect due to convective heat loss to the blood could leave a preserved cuff of tissue around the vessel.5–7 These findings were supported by the data of some case reports6–7 and an animal experimental model by using an air-filled balloon to occlude the CS.12 Furthermore, excessive RF energy could overcome the cooling capability and cause subsequent coronary artery injury and an occlusion in patients with preexistent coronary insufficiency,13,14 and the damage to the coronary artery due to the RF application may promote a new potential arrhythmogenic substrate. Hence, the knowledge in advance of an LCA at the MI is crucial to improve the outcome of the ablation and reduce any adverse complications due to unnecessary RF applications, and coronary visualization should be warranted in cases undergoing AF ablation targeting the MI.

The data from our study also demonstrated that a larger CS diameter was a significant independent related factor for an unsuccessful MI block line. A larger CS might also facilitate the promotion of a local cooling effect because of the increased vessel contact area along the MI line. A previous study demonstrated that additional CS ablation was frequently required during MI ablation in cases with a larger CS diameter,15 which might support the significance of the CS flow in the completion of an MI block line.

An LCA and the CS could also be assessed by computed tomography before the CA. To the best of our knowledge, there have been no comparative studies between coronary angiography and computed tomographic imaging for assessing the coronary arteries; however, the sensitivity of the computed tomographic imaging is not sufficient to detect small arteries because of the difficulty in identifying small arteries.16 On the other hand, coronary angiography could provide us with precise information about the coronary course, including the small coronary arteries, and the following CS staining image. From this point of view, coronary angiography may be a favorable method for assessing the LCF at the MI to accomplish a successful transmural block line and avoid any unnecessary RF applications in the MI region and the associated adverse procedural complications.

Other Possible Factors Affecting the MI Block Line
The accomplishment of creating a successful linear block line at the MI may also be influenced by other anatomical factors, because several complex structures, such as epicardial vessels and sleeves, are involved in this area. A previous study demonstrated that the structure of the vein of Marshall,17 high takeoffs of the left inferior PV,18 length of the MI line, and a pouchlike shape at the MI19,20 could be associated with the results of creating an MI block line.

In this study, a high amplitude of the local atrial potential seemed to lead to difficulty in creating a transmural block line at the MI. The significance of the local atrial potential on creating a transmural block line has also been demonstrated in cases undergoing tricuspid isthmus ablation.21 A high amplitude of the atrial potential may reflect local atrial thickness and/or partly include the far field component of an epicardial structure. In our data, clinical hypertension and the aging process also had a significant association on reducing the successful creation of a block line at the MI; thus, these factors might contribute to promoting the development of local hypertrophy at the MI.

Limitations
This study included some limitations. First, we had already observed the data from the coronary angiography before the ablation, and this might have led to a possible bias in creating the block line at the MI. Second, other factors, such as local myocardial thickness,22 morphological variations at the MI,19 and epicardial structure,17 could have affected the successful completion of the MI block line. A larger CS diameter was an independent related factor for predicting an unsuccessful MI block line in this study. However, it is possible that a larger CS diameter may have been an indirect surrogate index reflecting these confounding factors. Third, we did not perform any coronary angiography after the MI ablation and, therefore, the coronary injury due to the MI ablation could not be fully evaluated. Fourth, we could not determine the relationship...
between the LCA and gap conduction. However, an LCA significantly increased the incidence of the need for additional epicardial ablation from the CS inside, even in the patients with a successful MI block line; which might imply the importance of epicardial ablation from the CS inside, even in the patients with between the LCA and gap conduction. However, an LCA block line at the MI. The knowledge, in advance, of an LCA at the MI is crucial to improve the outcome of the ablation and reduce any adverse complications due to unnecessary radiofrequency applications, and coronary visualization should be warranted in cases undergoing AF ablation targeting the MI.

**Disclosures**

None.

**References**


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