Technique and Results of Linear Ablation at the Mitral Isthmus

Pierre Jais, MD; Mélèze Hocini, MD; Li-Fern Hsu, MBBS; Prashanthan Sanders, MBBS; Christophe Scavee, MD; Rukshen Weerasooriya, MBBS; Laurent Maclè, MD; Florence Raybaud, MD; Stéphane Garrigue, MD; Dipen C. Shah, MD; Philippe Le Metayer, MD; Jacques Clémenty, MD; Michel Haïssaguerre, MD

Background—This prospective clinical study evaluates the feasibility and efficacy of combined linear mitral isthmus ablation and pulmonary vein (PV) isolation in patients with paroxysmal atrial fibrillation (AF).

Methods and Results—One hundred consecutive patients (13 women; age 55±10 years) with drug-refractory, symptomatic paroxysmal AF underwent PV isolation and linear ablation of the cavitricuspid isthmus and the mitral isthmus (lateral mitral annulus to the left inferior PV). They were compared with 100 consecutive patients (14 women; age, 52±10 years) undergoing PV isolation and cavitricuspid ablation without mitral isthmus ablation. Bidirectional mitral isthmus block was confirmed by demonstrating (1) a parallel corridor of double potentials during coronary sinus (CS) pacing, (2) an activation detour by pacing either side of the line, and (3) differential pacing techniques. Isolation of all PVs and cavitricuspid isthmus ablation were performed successfully in all. Mitral isthmus block was achieved in 92 patients after 20±10 minutes of endocardial radiofrequency application and an additional 5±4 minutes of epicardial radiofrequency application from within the CS in 68, resulting in a conduction delay of 151±26 ms during CS pacing. Thirty-two patients with mitral isthmus ablation compared with 49 without (P=0.002) were arrhythmia free without antiarrhythmic drugs, mitral isthmus ablation being the only factor associated with long-term success (RR for AF recurrence, 0.2; CI, 0.1 to 0.4; P<0.001).

Conclusions—Catheter ablation of the mitral isthmus results consistently in demonstrable conduction block and is associated with a high cure rate for paroxysmal AF. (Circulation. 2004;110:2996-3002.)

Key Words: atrium • fibrillation • catheter ablation

Atrial fibrillation (AF) is frequently initiated by triggers from the pulmonary veins (PVs),1 leading to ablation aiming to electrically isolate these structures from the atria.2,3 Such procedures offer 57% to 70% success without antiarrhythmic drugs but are associated with a 20% to 60% recurrence rate as the result of lesion recovery, non-PV foci, or the need for further substrate modification. Previous surgical and catheter-based approaches have demonstrated that left atrial (LA) linear lesions were successful in substrate modification when complete block was achieved.6,7 The present study describes the technique of linear ablation at the mitral isthmus, defined as extending from the lateral mitral annulus to the ostium of the left inferior PV (LIPV), and the electrophysiological evaluation of conduction block at this site. Its efficacy in combination with PV isolation was compared with a group of patients with PV isolation alone.

Methods

Study Population
One hundred consecutive patients undergoing de novo ablation for symptomatic, drug-refractory paroxysmal AF were included from April to December 2002. These patients had ≥1 episode of AF every 10 days. PV electrical isolation and cavitricuspid and mitral isthmus ablation were performed. Their clinical outcome was compared with that of 100 consecutive patients undergoing ablation for the same indications, treated by PV electrical isolation and cavitricuspid ablation, without mitral isthmus ablation from April to December 2001. Both groups had comparable baseline characteristics (Table).

Electrophysiological Study
Written informed consent was obtained for all patients. Oral anticoagulation was administered (INR, 2 to 3) for ≥1 month before the procedure, and transesophageal echocardiography was performed to exclude LA thrombi.

A 6F quadrripolar or octapolar diagnostic catheter (Xtrem, Ela Medical, or Boston Scientific, respectively) was positioned in the coronary sinus (CS) for pacing and recording. The LA and PVs were accessed by means of a transseptal sheath (Preface, Biosense Webster) continuously perfused with heparinized 5% dextrose-water solution. Selective PV angiography was performed before and after ablation by hand injection of 5 to 10 mL of contrast through an NIH catheter. PVs were mapped with a circumferential 10-pole Lasso catheter (Biosense Webster). Surface ECG and intracardiac electrograms filtered at 30 to 500 Hz were recorded simultaneously with a...
polygraph (Bard Electrophysiology). A single bolus of 50 IU/kg of heparin was administered after the transseptal puncture and repeated only for procedures lasting ≥4 hours.

**Ablation Procedure**

PV isolation was performed 1 cm from the ostium of the right PVs as well as for the posterior and superior aspects of the left PVs to enhance efficacy and prevent PV stenosis in both groups. When ablation was required at the anterior portions of the left PVs, energy had to be delivered a few millimeters into the vein to achieve catheter stability. The procedural end point was isolation of the PVs, as determined by circumferential mapping. The isolation of all PVs was systematically performed in each patient without attempting to first demonstrate their arrhythmogenicity. Cavotricuspid isthmus ablation was then performed as previously described for accessory pathway ablation,8 suggesting of an epicardial gap. Ablation within the CS was performed as previously described for accessory pathway ablation,8 to demonstrate their arrhythmogenicity. Cavotricuspid isthmus ablation was then performed to achieve a bidirectional conduction block.

Ablation was performed by using a 4-mm, irrigated-tip catheter (Celsius Thermocool, Biosense Webster) with a flow rate (0.9% saline through the Cool Pump, Biosense Webster) titrated to achieve the desired power. PV ablation required a flow rate of 5 to 20 mL/min; isthmus ablation required up to 60 mL/min (2 mL/min between radiofrequency [RF] applications). Energy was delivered through a Stockert generator (Biosense Webster), with the temperature limited to 50°C and power of 20 to 30 W for PV and 50 W for cavotricuspid isthmus ablation. For the mitral isthmus, power delivery of 40 to 60 W was initially used. For safety reasons (explained below), the power used for cavotricuspid and mitral isthmuses was subsequently limited to 42 W.

**Mitral Isthmus Ablation: Technique and End Point**

The CS catheter was positioned to bracket the potential linear lesion between its proximal and distal bipoles. The ablation catheter, bent with a 90° to 180° curve and introduced through the long sheath to achieve good contact and stability, was first positioned at the ventricular edge of the lateral mitral annulus, where the atrioventricular electrogram showed a 1:1 to 2:1 ratio, to begin ablation. The sheath and catheter were then rotated clockwise to extend the lesion posteriorly, ending at the LIPV ostium (Figure 1). RF energy was delivered for 90 to 120 seconds at each site. The stability of the catheter was monitored during RF applications using electrograms and intermittent fluoroscopy to exclude inadvertent displacement, which could result in high-energy delivery within the LIPV ostium or LA appendage.

The effect of each RF application was assessed on the local electrogram during pacing from the proximal bipole of the CS catheter (located immediately septal of the line) to maximize conduction delay. Splitting of the local potentials resulting in an increase in the delay from the pacing artifact was considered evidence of an effective local lesion. After the initial attempt of creating this line, mapping was performed along the line to identify and ablate endocardial gaps, defined as sites showing the shortest delay between the pacing artifact and the local atrial potential, which could be single, narrow double, or fractionated (Figure 2B and C). If the initial attempt failed to produce complete block, ablation was performed in a more lateral position, at the base of the appendage.

Persisting epicardial conduction (Figure 3) was suspected when the linear lesion resulted in an endocardial conduction delay recorded on the ablation catheter but not on the adjacent distal bipole of the CS catheter (lateral of the line). The ablation catheter was then withdrawn from the LA and introduced into the CS to map the epicardial side of the isthmus and identify fractionated or early potentials suggestive of an epicardial gap. Ablation within the CS was performed as previously described for accessory pathway ablation,8 with a flow rate of 17 to 60 mL/min, target temperature of 50°C, and power of 20 to 30 W. All patients subsequently underwent exercise.

**Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>PV Isolation With Mitral Isthmus Ablation (n=100)</th>
<th>PV Isolation Without Mitral Isthmus Ablation (n=100)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>55±10</td>
<td>52±10</td>
<td>0.23</td>
</tr>
<tr>
<td>Women</td>
<td>13</td>
<td>14</td>
<td>0.81</td>
</tr>
<tr>
<td>Duration of AF, y</td>
<td>6±6</td>
<td>7±6</td>
<td>0.52</td>
</tr>
<tr>
<td>Failed antiarrhythmic drugs, No.</td>
<td>4±2</td>
<td>4±2</td>
<td>0.27</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>24</td>
<td>22</td>
<td>0.77</td>
</tr>
<tr>
<td>LA diameter, mm</td>
<td>46±6</td>
<td>45±6</td>
<td>0.69</td>
</tr>
<tr>
<td>LV end-diastolic diameter, mm</td>
<td>53±6</td>
<td>51±5</td>
<td>0.31</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>71±11</td>
<td>70±12</td>
<td>0.72</td>
</tr>
</tbody>
</table>

**Figure 1.** Anteroposterior (AP) and left anterior oblique (LAO) views of catheter placement during mitral isthmus ablation. Ablation was started with the ablation catheter at the ventricular edge of the mitral annulus (1). The catheter was then moved gradually to mid-isthmus (2) and subsequently to the junction with the ostium of the LIPV (3). A long sheath was used to facilitate catheter manipulation.
stress testing to exclude potential symptomatic coronary artery injury, and in a subset of 15 consenting patients, coronary angiography was performed to exclude asymptomatic coronary artery injury resulting from ablation.

To evaluate possible effects on LA conduction caused by ablation, the surface ECG was scrutinized for changes in P-wave morphology, and the sinus activation time at the mitral isthmus (P-A interval; onset of the P wave in lead II to the atrial potential on the mitral isthmus) was measured before and after ablation.

**Confirmation of Mitral Isthmus Block**

The end point of ablation was the achievement of bidirectional mitral isthmus block demonstrated by using criteria similar to that previously described for cavotricuspid isthmus block:

1. The presence of widely separated local double potentials along the length of the ablation line during CS pacing septal of the line.
2. Mapping the activation detour during pacing from either side of the line. Pacing on the septal side of the line via the CS demonstrates activation toward the line both septally and laterally.
3. Differential pacing to distinguish slow conduction across the isthmus from complete block. With the distal bipole of the CS catheter placed just septal to the linear lesion, the pacing site was changed from the distal to proximal bipole of the CS catheter without moving any of the catheters (Figure 5). Stimulus-to-electrogram timing was measured to the same point on the matching electrogram component before and after changing the pacing site. With complete block, the stimulus-to-electrogram timing was shortened after shifting the pacing site from the distal to the proximal bipole.

**Postablation Management and Follow-Up**

Subcutaneous heparin was administered after ablation to maintain a partial thromboplastin time of 2 to 3 times the control value. Patients were monitored in the hospital for 4 to 5 days by telemetry or Holter.
recordings and daily 12-lead ECGs. Exercise stress testing for 
ischemia and transthoracic echocardiography were performed before 
discharge.

Patients were discharged on oral anticoagulant for 1 to 3 months, 
which was then stopped in the absence of recurrence. They were 
hospitalized for 2 days at 1, 3, 6, and 12 months after the last (or last 
repeat) procedure for follow-up assessment involving transthoracic 
echocardiography, Holter recordings, stress testing, and a high-
resolution CT scan of the PVs at 1 year. For the purpose of this study, 
follow-up was interrupted after 12 months in both groups to allow 
comparison over the same period of time. A successful outcome was 
declared as the absence of AF without the use of antiarrhythmic 

Statistical Analysis
All variables are reported as mean±SD. Comparison between groups 
was performed with either the Student t test or Wilcoxon rank sum 
test. Proportions were compared by using the Fisher exact test. The 
relation between baseline parameters and outcome was assessed with 
a descending stepwise Cox proportional hazards model and reported 
as the relative risk with 95% confidence intervals. Statistical signif-
icance was established at P<0.05.

Results

Procedural Outcome
All PVs were successfully disconnected in all patients without 
complications. Ablation of the endocardial aspect of the 
mitral isthmus was performed with the use of 20±10 minutes 
of RF energy and resulted in complete bidirectional block in 
32 patients (32%); >30 minutes of RF had to be delivered in 20 
patients. In 68 patients (68%), persisting epicardial conduction 
after endocardial ablation was evidenced by early 
electrograms with high voltage in the CS contrasting with the 
corresponding endocardial aspect (Figure 3). In 3 of these 
patients, catheter manipulation in the CS produced mechanical 
ischmus block. Ablation from within the CS (Figure 3) 
resulted in complete isthmus block in 57 (84%) with the use 
of a mean of 5±4 minutes of RF energy. However, in 3 
patients (3%), RF energy could not be delivered epicardially, 
as it was impossible to advance the ablation catheter in the CS 
to a site of sufficient proximity to the ablation line.

Bidirectional mitral isthmus block was achieved in 92 
patients (92%). Procedure duration, fluoroscopy time, and 
total RF delivery time were 179±56, 51±21 and 65±26 
minutes, respectively.

Electrophysiology of the Mitral Isthmus
The creation of a complete isthmus block resulted in an 
activation delay of 151±26 ms (range, 104 to 228 ms) during
CS pacing. This delay corresponded to the time required for activation to proceed around the mitral annulus and reach the lateral flank of the line (Figure 6C). Another activation front was observed to ascend from the CS pacing site along the posterior wall between the right and left PVs and pass around the LA appendage to finally collide with the perimitral front on the lateral flank of the ablation line. When the pacing site was shifted from the distal to proximal bipole on the CS catheter (differential pacing), the interval from the pacing artifact to the terminal potential was reduced by a mean of 15±9 ms, confirming conduction block along the mitral isthmus.

With endocardial pacing lateral to the ablation line, a similar delay of 150±32 ms to the CS potential septal to the line with proximal-to-distal activation sequence was observed, confirming bidirectional block and complete detour of activation around the mitral annulus. Unidirectional block was not observed.

In contrast to the considerable delay evidenced during CS pacing, there was no conduction delay during sinus rhythm, demonstrated by the absence of significant change in the P-A interval measured at the mitral isthmus (105±18 versus 111±18 ms; P=NS) and P-wave morphology with ablation.

Clinical Outcome
Thirty-two patients (32%) who underwent mitral isthmus ablation had ≥1 recurrence of atrial arrhythmia as compared with 49 patients (49%) treated with PV isolation alone (P=0.02). All 32 patients with recurrent arrhythmia underwent a second procedure with 4 requiring a third one (total 36 procedures).

Organized atrial arrhythmias were present at the commencement of 14 procedures. LA macroreentry as defined by activation and entrainment mapping and/or electroanatomic mapping was observed to occur through an incomplete or recovered mitral isthmus line in 5 (Figure 6) or around the right PVs in 4 patients. These were successfully ablated by RF application at gaps along the mitral isthmus or with a linear lesion along the LA roof connecting the 2 superior PVs. Cavotricuspid isthmus–dependent flutter was observed in 2 patients. In 3 patients, a regular monomorphic atrial tachycardia was observed in the presence of mitral isthmus block. These arrhythmias could not be entrained from the roof or posterior LA and were confirmed to have a focal origin by ablation at the posterior LA in one and from a recovered right and left superior PV in the other 2.

In 22 procedures, reablation was performed for AF recurrence. Conduction recovery was observed in ≥1 PV in all patients and non-PV foci (not observed during the index procedure) were identified in 12; in the RA: posterior (3), lateral (1), or in the CS (2) or the LA: septum (3) posterior (1) inferior (1) or roof (2).

At 1 year after the last procedure, 87 patients (87%) undergoing mitral isthmus ablation were arrhythmia free.
without the need for antiarrhythmic drugs compared with 69% of those treated by PV isolation only \((P=0.002)\). In patients with recurrent arrhythmia, structural heart disease was observed more frequently \((36\% \text{ versus } 20\%, \ P=0.02)\). On multivariate analysis, only mitral isthmus ablation was associated with success without drugs \((\text{relative risk for AF recurrence, } 0.2; \text{ CI, } 0.1 \text{ to } 0.4; \ P<0.001)\).

**Complications and Safety Issues**

During the 136 procedures performed in patients undergoing mitral isthmus ablation, no significant PV stenosis \(\text{(acutely or at } 1 \text{ year)}\) or thromboembolic complications were observed. Cardiac tamponade occurred in 4 patients \((4\%)\). Three were preceded by an audible pop: 1 during cavotricuspid isthmus ablation with a delivered power of 48 W and 2 during endocardial RF delivery at the mitral isthmus with a delivered power \(>50 \text{ W}\). The fourth was attributed to catheter manipulation in the LA during mitral isthmus ablation. All were drained percutaneously without long-term sequelae. In the last 25 patients, the delivered power was limited to 42 W and there were no further cases of tamponade.

No complications were attributable to ablation within the CS. There was no evidence of coronary artery involvement in any patient either clinically or on stress testing during follow-up. In addition, coronary angiography was performed after ablation in 15 patients without detectable abnormality, particularly at the segment of the circumflex artery adjacent to the line of ablation.

**Discussion**

This study presents new information about the feasibility and role of linear ablation at the mitral isthmus in the ablation of AF. It describes the technique and rigorous validation criteria for the evaluation of conduction block at the mitral isthmus, which can be achieved in 92% of patients and was associated with 87% being arrhythmia free without the use of antiarrhythmic drugs.

PV isolation for paroxysmal AF has been shown to be effective and safe, but the success rate is limited to approximately 70%\(^2,4\) because of the presence of non-PV foci and persistence of the substrate for AF. LA linear lesions at various locations have been demonstrated to modify the substrate and prevent the clinical occurrence of AF, particularly when complete linear block is achieved.\(^6,7\) However, the ideal number and positions of linear lesions are unknown.

Emerging evidence implicates regions of conduction slowing and block associated with atrial remodeling in the substrate predisposing to AF. In the LA, recent studies have demonstrated preferential propagation that is closely correlated with muscle fiber orientation along the posterior LA and circumferentially around the mitral annulus.\(^10,11\) In addition, the mitral isthmus has been demonstrated to be a site of intra-atrial conduction block during the ablation of accessory pathways.\(^12\) Such preferential propagation occurring in response to functional or anatomic conduction block \(\text{(perhaps exacerbated by AF or conditions predisposing to AF)}\) is capable of facilitating reentry, utilizing the mitral isthmus, as recognized with common forms of LA macroreentry,\(^13\) and thus may have a role in the milieu that maintains AF.

An essential requirement for the creation of complete linear lesions is that it bridges anatomic structures to provide a contiguous line of conduction block capable of preventing the persistence of reentrant wavelets. There are, however, only a limited number of structures within the LA that are able to anchor such lesions. Previous attempts at such linear ablation have been limited in the achievement of contiguous conduction block by the technical challenge of creating such long linear lesions and by the uncertainty of the ablation end point.

Ablation of the mitral isthmus as described in the present study has several inherent advantages compared with previous attempts at linear ablation within the LA. First, the mitral isthmus is short \((2 \text{ to } 4 \text{ cm})\), anatomically bounded by the mitral annulus, LIPV ostium, and superiorly by the LA appendage. Although being short and therefore less likely to result in conduction gaps, its contiguity with the left PVs and appendage results in, functionally, a long line of conduction block that transects the lateral LA from the mitral annulus to the roof, as evidenced by the significant activation detour observed in the present study. Its electrophysiological consequences could be considered analogous to the results achieved by cavotricuspid isthmus ablation, where a short line is amplified by the crista terminalis to result in a long line of functional conduction block. It is thus likely that the ablation strategy used in the present study modifies a large region of the LA substrate for AF by eliminating anatomic or functional reentry involving the mitral isthmus or PVs. Additionally, it may eliminate arrhythmogenic triggers arising from the ligament of Marshall.

Second, unlike most other lines studied within the LA, mitral isthmus ablation has a well-defined demonstrable procedural end point of bidirectional conduction block, again analogous to cavotricuspid isthmus ablation. Validation of conduction block is greatly facilitated by its proximity to the CS, allowing pacing and recording on either side of the line to confirm bidirectional block. Differential pacing can also be performed to exclude slow conduction through an incomplete line. In the present study, complete block could be demonstrated in 92% of the cases, compared with 30% and 56% in previous studies involving other lines.\(^6,7\) and resulted in 87% of patients being arrhythmia free without the use of antiarrhythmic drugs.

Finally, despite the significant activation detour during pacing adjacent to the ablation line, there was no alteration of LA activation during sinus rhythm, reflecting the observation that this region represents the latest atrial activation during sinus rhythm \(\text{(Figure 7)}\). Preserved LA activation during sinus rhythm is a desirable end point to enhance the recovery of atrial mechanical function after restoration of sinus rhythm.

**Limitations**

Achievement of complete block required \(>30 \text{ minutes of RF delivery}\) in 20 patients. This may be due to the thickness of local atrial tissue and/or to the blood flow of the coronary sinus, which by reducing conductive heating may prevent transmural lesions. The need for ablation from within the CS in 68% may be considered a limitation, but with delivered
power limited to 20 to 30 W; as for accessory pathway ablation, no adverse consequence was observed.8

A 4% incidence of cardiac tamponade was observed in the early phase of the study and was attributed to catheter manipulation or ablation using >45 W of power. No further cases occurred after the power was limited to ≤42 W. Finally, though the study was nonrandomized, we have tried to minimize bias by using consecutive patients and similar PV isolation techniques in both groups; nevertheless, a future prospective, randomized evaluation would be desirable.

Conclusions
Catheter ablation of the mitral isthmus with a procedural end point of bidirectional conduction block is achievable in 92% of patients. Used in conjunction with PV isolation, this linear lesion is associated with a high cure rate for paroxysmal AF while preserving atrial activation during sinus rhythm.

References
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