Transthoracic epicardial ablation of mitral isthmus for treatment of recurrent perimitral flutter

Antonio Berruezo, MD, PhD, † Felipe Bisbal, MD, †† Juan Fernández-Armenta, MD, †† Naiara Calvo, MD, PhD, † José Ángel Cabrera, MD, PhD, ‡ Damián Sanchez-Quintana, MD, PhD, § David Andreu, MSc, † Teresa M. de Caralt, MD, PhD, † Josep Brugada, MD, PhD, †† Lluís Mont, MD, PhD ††

From the † † Unitat de Fibril·lació Auricular (UFA), Cardiology Department, Hospital Clinic, Universitat de Barcelona, Barcelona, Spain, † Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain, ‡ Department of Cardiology, Hospital Universitario Quirón-Madrid, Madrid, Spain, and § Department of Anatomy and Cell Biology, University of Extremadura, Badajoz, Spain.

BACKGROUND Perimitral flutter (PMF) is a common form of left atrial tachycardia after atrial fibrillation (AF) ablation. The mitral isthmus (MI) is the standard ablation target. However, in some cases bidirectional block cannot be achieved.

OBJECTIVE The purpose of this study was to describe the first experience using a transthoracic epicardial (TTE) approach to treat recurrent PMF after prior unsuccessful ablation.

METHODS This is a case series of four patients with recurrence of highly symptomatic drug-refractory PMF (all male, median age 55 years, 3/4 hypertensive, 2/4 persistent AF, median AF period 24 months). Three patients presented with PMF-related tachymyocardiopathy. TTE ablation of MI was performed after a median of two prior endocardial MI and coronary sinus ablation attempts, using an open-tip 3.5-mm irrigated catheter (40 W, 45°C). Persistent bidirectional block was assessed by activation mapping and differential pacing and was achieved in all patients.

RESULTS No PMF recurrence was observed after median follow-up of 18 months (range 15–22 months; two patients without antiarrhythmic drugs and two with previously ineffective amiodarone). Left ventricular function normalized in all three patients with tachymyocardiomyopathy. There were no complications related to TTE approach.

CONCLUSION The present study is the first to report the feasibility of a TTE approach for highly symptomatic PMF refractory to endocardial and coronary sinus MI ablation.

KEYWORDS Perimitral flutter; Transthoracic epicardial approach; Catheter ablation; Mitral isthmus line

ABBREVIATIONS AF = atrial fibrillation; CS = coronary sinus; IQR = interquartile range; LAT = left atrial tachycardia; LMWH = low-molecular-weight heparin; MI = mitral isthmus; PMF = perimitral flutter; PV = pulmonary vein; PVI = pulmonary vein isolation; RF = radiofrequency; TTE = transthoracic epicardial

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Introduction

Catheter ablation of atrial fibrillation (AF) has become a well-established therapy for symptomatic drug-resistant AF, and the number of procedures has grown in the last decade. Although ablation technique has evolved considerably and the safety profile has improved,1,2,3 recurrences of atrial arrhythmias are still a great concern.4,5 To improve outcomes, strategies aiming to modify the substrate have been introduced, such as additional roof or mitral isthmus (MI) lines.4,5 However, the outcome benefit of this strategy is controversial because of its potential proarrhythmic role.6–8

Left atrial tachycardia (LAT) has been described as a complication of AF ablation.9,10,11 This arrhythmia usually is persistent, with very limited response to antiarrhythmic medications, and is often associated with rapid ventricular rates that produce generally severe symptoms and even left ventricular function impairment.

Perimitral flutter (PMF) is a common form of LAT, especially after AF ablation.4 Ablation of the MI between the inferolateral aspect of the mitral annulus and the ostium of the left inferior pulmonary vein is the standard strategy for ablation of the arrhythmia. The great challenge of this technique is creation of a complete transmural line to achieve bidirectional conduction block. However, probably because of the complex anatomy of this region, in many cases this end-point cannot be accomplished. Moreover, the creation of lesions leading to incomplete block with slow residual conduction may result in incessant LATS, which often are difficult to cure.4,11,12 Ablation of MI within the coronary sinus (CS) and other techniques have been proposed as a means to achieve better results.13–16

Address reprint requests and correspondence: Dr. Antonio Berruezo, Arrhythmia Section, Cardiology Department, Hospital Clinic, Villarroel, 171, Barcelona, Spain. E-mail address: berruezo@clinic.ub.es.
The present study describes the first experience with a new transthoracic epicardial (TTE) ablation of the MI in patients with highly symptomatic recurrent PMF after prior unsuccessful endocardial approach.

Methods

Study population

This is a case series of four patients with prior AF ablation presenting with recurrence of highly symptomatic and drug-refractory PMF after unsuccessful endocardial and CS MI ablation. Written informed consent was obtained from all participants. The study protocol was approved by the hospital’s Ethics Committee.

Previous AF ablation procedure

Prior to the ablation procedures, transesophageal echocardiography was performed. Patients discontinued oral anticoagulation 2 days before the procedure, and low-molecular-weight heparin (LMWH) was administered until the day before the ablation. Echocardiography was performed immediately after the procedure to rule out residual pericardial effusion. Anticoagulation was then reinitiated with LMWH and acenocoumarol. LMWH was interrupted when international normalized ratio \( \geq 2 \).

Circumferential pulmonary vein isolation (PVI) was the first ablation procedure in all the cases, as described elsewhere. A three-dimensional map was constructed using an electroanatomic mapping system (CARTO, Biosense Webster, Diamond Bar, CA). Magnetic resonance angiographic images were integrated into the navigation system. Continuous radiofrequency (RF) lesions surrounding each ipsilateral PV were delivered. The end-point was entrance and exit block inside the entire surrounded region, which was checked with a circular mapping catheter and by pacing within the PV ostia. A roof line was performed in patients 1 and 2 to join contralateral encircling lesions, with an additional MI line from the inferolateral aspect of the left inferior PV to the mitral annulus. These patients did not present spontaneous or inducible organized atrial arrhythmias during the procedure, and the lines were performed empirically.

In repeated procedures, PV reconnection was initially evaluated. If reconnected, ablation of gaps in the circumferential lines was performed using a Lasso catheter to guide mapping, until bidirectional conduction block within PV ostia was achieved. If LAT was present, macroreentrant atrial tachycardia circuits were identified by entrainment maneuvers and activation mapping in all four cases.

Endocardial MI ablation

A 20-polar catheter (Halo, Cordis-Webster, Diamond Bar, CA) was placed in the CS, with the proximal poles located close to the CS ostium. If atrial flutter was the presenting rhythm, overdrive atrial pacing was performed from the different CS dipoles to determine their location relative to the tachycardia circuit and to exclude right atrial flutter. If the patient was in sinus rhythm, atrial flutter was induced by rapid burst pacing from the right atrium, followed by entrainment maneuvers. If LAT flutter was confirmed, a transeptal access and electroanatomic mapping were performed as described earlier.

After PMF was confirmed by entrainment and activation mapping, an endocardial MI line was performed using an irrigated-tip thermocouple-equipped catheter (NaviStar, Biosense Webster), with target temperature of 45°C and 40 W. In one case, PMF interruption occurred, without bidirectional conduction block across the MI line. In all cases, ablation within the CS was performed, with target temperature of 45°C and maximum output of 25 W. In two cases, an additional endocardial MI ablation line was performed during CS occlusion with a balloon catheter (Arrow International Inc, PA), which was positioned in the lateral CS/great cardiac vein, distal to the MI line. The balloon was fully inflated under fluoroscopy, and MI ablation was then performed as described earlier.

TTE ablation procedure

Prior to the procedure, patients underwent contrast-enhanced cardiac computed tomography or contrast-enhanced magnetic resonance angiography. Image integration with the electroanatomic mapping was performed using the left atrium in three patients and the right atrium in one patient. After the fusion achieved sufficient accuracy, images were used to guide ablation, evaluating the location and features of the MI and pulmonary veins and vessels. Coronary angiography was not used during the procedure. Periprocedural management of anticoagulation was performed as in the previous procedures. Transesophageal echocardiography was performed before the ablation procedure to rule out the presence of thrombus in the left atrial appendage. Unfractionated heparin was administered (bolus 100 UI/kg, maximum dose 6000 UI) at the time of the transeptal puncture and additional doses during the procedure to maintain activated clotting time between 250 and 350 seconds.

The TTE access protocol was performed as previously described. In summary, an epidural needle (Perican, Braun, Germany) was introduced through the subxyphoid space into the pericardial space at an angle of 30° to 45°, guided by fluoroscopy and contrast. A floppy-tip guidewire was then advanced to completely surround the cardiac silhouette. A deflectable sheath (Agilis, St. Jude Medical, MN, USA) was used to facilitate mapping and obtain a stable position during RF delivery.

The perimital reentrant circuit was demarcated by activation mapping and confirmed by entrainment maneuvers (Figure 1). The appropriate RF delivery target was determined as follows: (1) anatomic identification of the MI, (2) endocardial delivery of RF lesions, and (3) voltage map scanning to identify the zone with the lowest-voltage electrograms (Figures 2 and 3). Along the previously identified target area for the MI line, RF ablation lesions were created epicardially with an irrigated-tip, thermocouple-equipped catheter (NaviStar, Biosense Webster, CA), with the same temperature setting and energy output as used endocardially. After completing RF ablation, a new activation map was performed during
pacing from dipoles at each side of the ablation line. Bidirectional block of the MI line was confirmed by activation maps, double potentials along the ablation line, and differential pacing (Figure 4). To ensure persistent block, maneuvers were repeated after at least a 30-minute waiting period. A burst pacing after ablation was performed to check for PMF inducibility in all cases. The pericardial access was removed immediately after the procedure, after draining the pericardial cavity, and no drainage was left after the procedure.

**Follow-up**

Patients were followed up at 3, 6, and 12 months after the ablation and whenever required because of symptoms. A 48-hour Holter monitoring was obtained before each visit, and patients were asked to report any episode of documented AF or symptoms. All patients continued oral anticoagulation for a minimum of 2 months. All four patients received antiarrhythmic drugs (flecainide in the absence of left ventricular dysfunction, amiodarone otherwise) during at least the first 12 weeks after ablation and longer as needed because of recurrences. Presence of AF or flutter lasting > 30 seconds after a 3-month blanking period was considered procedural failure.

**Results**

**Patient characteristics**

A series of four patients were included (all male, median age 55 years, 50% with persistent AF, median AF period 24 months). Patients’ baseline characteristics are listed in Table 1.

All patients underwent PVI as the first approach. Additional roof and mitral lines were deployed in both patients with persistent AF. After a median of 158 (163) days, all patients had highly symptomatic recurrences (LAT in patients 1 and 2 who had prior roof and mitral lines, and AF in patients 3 and 4; patient 4 also presented with typical atrial flutter). Tachycardia-induced left ventricular dysfunction occurred in three patients.
Repeated procedures were performed in all patients before the subxyphoid epicardial approach was considered. Patients 2 and 4 had one repeated procedure, and patients 1 and 3 had two procedures. Reconnection of at least one PV was observed in all patients. After reisolation, PMF was induced in patients 1 and 2, and a mitral line was again
performed endocardially and through the CS, without achieving bidirectional block (Table 2). All patients recurred with a highly symptomatic PMF after the second procedure.

Anatomy of MI, circumflex artery, and CS
Anatomy of the MI and related structures was analyzed from the preprocedure cardiac computed tomography or magnetic resonance angiography. Median length [interquartile range (IQR)] of the MI was 32 (8.6) mm. The median (IQR) value for the maximum thickness of the MI was 3.3 (1.4) mm. The maximum thickness of the left atrial wall was located at a median (IQR) of 20.5 (9.5) mm from the AV groove. In all cases, the point of maximum thickness was above the CS and circumflex artery. In three of four patients, the circumflex artery was analyzed from proximal CS demonstrates conduction through the MI before epicardial ablation (A). Bidirectional conduction block is demonstrated when pacing from both sites of the MI line (B, C). Note the presence of double potentials at the site of the MI line (arrows). PA = posteroanterior.

Table 1 Patients’ baseline and first PVI characteristics

<table>
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<tr>
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<th>Age (years)</th>
<th>Sex</th>
<th>HT</th>
<th>AF type</th>
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<th>EF</th>
<th>AF duration (minutes)</th>
<th>First ablation</th>
<th>Time to recurrence (minutes)</th>
<th>Type recurrence</th>
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AF = atrial fibrillation; AFL = atrial flutter; EF = ejection fraction; HT = hypertension; LAD = left atrial diameter; LAT = left atrial tachycardia; ML = mitral line; Pr = persistent; Px = paroxysmal; PVI = pulmonary vein isolation; RL = roof line; TMP = tachymyocardiopathy.
artery was located between the mitral annulus and great cardiac vein (GCV) at the posterior MI.

TTE ablation of MI
A median of 2 (1–3) endocardial MI ablation attempts, together with unsuccessful CS ablation, were made before attempting epicardial ablation. Bidirectional conduction block of the MI was achieved in all patients after a mean of 217 ± 37 seconds of epicardial RF application. In two patients, PMF stopped after ablation was completed (Figure 5). The other two patients presented another macroreentrant LAT after achieving MI bidirectional block and required additional RF application in other sites (septum and CS ostium) (Table 3).

Procedural time and complications
The epicardial approach increased the mean procedural time compared to prior endocardial MI ablation (135 ± 30 minutes vs 255 ± 44 minutes, respectively, \( P = .015 \)). Fluoroscopy time did not differ by approach (23 minutes vs 22 minutes, respectively, \( P = .688 \)). One patient presented with peri-procedural transient ischemic accident after the second ablation procedure, with rapid and complete recovery. There were no complications related to the epicardial access and ablation procedure.

Clinical outcome
After median follow-up of 18 (15–22) months, three patients had no recurrences after a 3-month blanking period without antiarrhythmic drugs. Patient 4 remained asymptomatic under previously ineffective amiodarone. At 6 months, all thee patients with PMF-induced tachymyocardiopathy showed normalization of left ventricular ejection fraction.

Discussion
In the present study, we describe the initial experience performing a TTE approach to ablate the MI in patients with highly symptomatic PMF, after previous unsuccessful endocardial and CS ablation. The end-point of persistent bidirectional conduction block was achieved in all four patients, showing that this technique is feasible, safe, and effective.

PMF is a prevalent form of macroreentrant LAT. The widespread use of catheter ablation of AF has increased PMF incidence, with reports ranging from 2.6% to 76%. The
MI line, which connects the posterolateral mitral annulus with the left inferior PV, is the current standard ablation strategy for treatment of this arrhythmia; however, the reported rate of acute bidirectional block remains low (31%–92%). Recently, Hocini et al reported successful block rates of 65% and 68% when ablating epicardially within the CS with and without spot CS occlusion, respectively (P = NS). The lack of complete bidirectional block has been associated with LAT recurrence. Thus, complete block is the cornerstone of the ablation strategy in patients with drug-refractory PMF. Nevertheless, it remains one of the most difficult challenges in modern electrophysiology.

**MI anatomy and endocardial ablation**

CS muscle sleeves have been reported in up to 75% of patients; they insert into the left atrium below the AV groove and occasionally extend onto the mitral valve. Most of these sleeves can be targeted when ablating within the CS. However, TTE ablation probably does not contribute to targeting this structure. On the other hand, anatomic and histologic studies have shown wide variations of left atrial wall thickness along the MI, with a mean value of 3.8 mm and maximum thickness up to 7.7 mm, which might prevent the transmurality of the lesions. As observed in all cases of the present series, the area of maximum thickness can be located above the CS, making it impossible to reach the epicardial aspect of this area from the CS. In this setting, the transmorphic approach allows ablation of the epicardium of this region to achieve transmural lesion and MI block.

Alternative locations for RF delivery include an anterior or septal MI line. Tzeis et al demonstrated that a modified anterior line extending from the anterior/anterolateral mitral annulus to the ostium of the left superior PV resulted in change or termination of PMF in 96.9% of cases, and bidirectional block across the line could be demonstrated acutely in 86% of patients. They proposed this novel linear lesion as a safe first-line approach for PMF or, at least, as a backup approach when ablation deep within the CS was not feasible for completion of an MI line. Sanders et al had previously reported only 58% complete linear lesions when combining a roof line with a medial anterior line connecting the mitral annulus and the right superior PV or the septal part of the roof line. The authors reported macroreentrant LAT through incomplete or recovered gaps in some patients of the series. Recently, Wong et al reported resumption of conduction through the MI line in up to 29% of patients after ablation using a steerable sheath and high output power.

In summary, despite the development of new ablation techniques, incomplete conduction block or resumption of conduction through the MI line is observed in a substantial proportion of patients. The lack of transmural lesions might play a key role in this scenario. The TTE approach can help when transmural lesion is not achieved endocardially or by ablating within the CS.

**Role of CS and circumflex artery**

Histologic studies have demonstrated a variable relationship between the position of the CS and the mitral annulus. In a histologic study, Becker showed that great cardiac vein but not CS was present in the MI section in all cases. The CS runs along the atrial side of the mitral annulus, at a distance ranging from 6 to 11 mm. Some reports have described that epicardial ablation within the CS is required in a high percentage (67%–97%) of patients to achieve complete block. If the linear ablation is carried down only from the CS catheter, a gap could result between the CS and mitral annulus. In addition, the blood flow of the CS and the circumflex coronary artery have a cooling effect, acting as a heat sink and attenuating transmural lesion formation. Recent studies have hypothesized that balloon occlusion of the CS would reduce this effect and decrease the need for CS ablation. However, CS occlusion did not improve the overall rate of acute MI block. In a study by Wong et al, MI length was a predictor of failure to achieve MI block. Furthermore, only 25% of patients obtaining bidirectional conduction block with CS balloon occlusion had persistent block during follow-up. These results suggest that a heat sink effect may not be the only obstacle to achieving complete MI ablation and that anatomy may play a role in catheter stability and contact. Therefore, although ablation within the CS improves the outcome, complete MI block is still a challenging issue and cannot always be achieved.

**TTE ablation of MI**

The present study demonstrated for the first time how bidirectional conduction block across the MI line can be achieved through a TTE approach in patients with up to three previous unsuccessful ablation procedures. Interestingly, multiple epicardial low-voltage fractionated electrograms were observed. This is probably related to nontransmural

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**Table 3** Index procedure (transthoracic epicardial approach)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Procedural time (minutes)</th>
<th>Rx Time (minutes)</th>
<th>PMF cycle length (ms)</th>
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<th>Epi ML</th>
<th>Rhythm after TTE ML</th>
<th>Additional ablation sites</th>
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<th>Recurrence</th>
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AAD = Antiarrhythmic drugs; CS = coronary sinus; EF = left ventricular ejection fraction; L = inferolateral line (left inferior pulmonary vein–inferior mitral annulus); LAT = left atrial tachycardia; MI = mitral isthmus; ML = mitral line; PMF = perimital flutter; SR = sinus rhythm; TTE = transthoracic epicardial.
endocardial lesions that could be the substrate sustaining the PMF. RF delivery at these sites led to conduction block. On the other hand, the mean procedural duration was longer when the additional TTE approach was performed. However, mean fluoroscopic times did not increase and there were no complications, indicating that this approach has the potential to be a safe and feasible procedure.

The TTE approach can be considered an option in the subset of patients with symptomatic and recurrent PMF after unsuccessful endocardial and CS ablation. However, this technique should only be performed by an operator who is highly experienced in using this approach.

**Study limitations**
Some limitations should be acknowledged. First, the number of patients is too small to firmly establish the safety of the procedure. Lesion of the phrenic nerve has been reported to be a complication of epicardial ablation. Nevertheless, this complication could be prevented by infusing saline in the pericardial space.

**Conclusion**
The present study is the first to report the feasibility of the TTE approach for PMF ablation. This technique may achieve complete MI block and may be considered by experienced operators for use in highly symptomatic patients with prior unsuccessful endocardial and CS ablation.

**References**