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Alternative strategies to improve success rate of mitral isthmus block

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Abstract

Achieving bidirectional conduction block (BDB) across the mitral isthmus (MI) is technically challenging. We describe our experience using different ablation strategies for achieving successful MI block.

We reviewed the records of patients who had undergone MI ablation for peri-mitral (PM) flutter at our institution from January 2010 to May 2015. We investigated ablation strategies for achieving MI block and their long-term outcomes in terms of recurrence of atrial tachyarrhythmia.

Single endocardial MI ablation with or without distal coronary sinus (CS) ablation achieved MI block in 129 out of 236 (54.7%) patients. After failure of MI block, a new MI line ablation, ablation targeting the vein of Marshall (VOM), or anterior line ablation was performed in selected patients. The MI block was achieved in 13 (52.0%) out of 25 patients with new MI line ablation and in 13 (68.4%) out of 19 patients with VOM ablation. Anterior line ablation was tried in 23 patients and the line of block was achieved in 12 (52.2%) patients. Finally, overall PM BDB (PMB, MI block or anterior line block) was achieved in 167 (70.8%) of 236 patients. The incidence atrial tachyarrhythmia was similar between the patients with successful PMB and those with failed PMB (32.9% vs 42.0%, P=.18). In multivariable Cox regression analysis, the PMB was not associated with recurrence of atrial tachyarrhythmia (hazard ratio [HR]: 0.70, 95% confidence interval [CI]: 0.43–1.12).

In conclusion, single endocardial MI line with or without distal CS ablation showed limited success for achieving MI block. Additional substrate modifications such as a new MI line ablation, anterior line ablation, or ablation targeting the VOM may improve the success rate of PMB block. However, the benefits of PMB were not clear in this study.

Abbreviations: AF = atrial fibrillation, AFL = atrial flutter, BDB = bidirectional conduction block, CI = confidence interval, CS = coronary sinus, HR = hazard ratio, LA = left atrium, LAA = left atrial appendage, MI = mitral isthmus, PM = peri-mitral, PV = pulmonary vein, PVI = pulmonary vein isolation, RF = radiofrequency, VOM = vein of Marshall.

Keywords: atrial fibrillation, atrial flutter, mitral isthmus, radiofrequency

1. Introduction

Macro-reentrant tachycardia is a major cause of atrial tachyarrhythmia recurrence after pulmonary vein (PV) isolation (PVI) for atrial fibrillation (AF). Perimitral (PM) atrial flutter (AFL) revolving around the mitral annulus is reportedly the most common pattern of tachycardia, accounting for approximately 50% of total macro-reentrant tachycardia.[1–3] Radiofrequency (RF) catheter ablation is often required to treat PM AFLs. Linear ablation with bidirectional conduction block (BDB) achievement is essential to treat PM AFLs. Traditionally, the mitral isthmus (MI) has been the preferred target area for creation of BDB for PM AFLs.

The MI is defined as the lateral left atrial (LA) region extending from the lateral mitral annulus to the left inferior PV ostium. Previously, MI ablation and PVI had improved the maintenance of sinus rhythm in patients with paroxysmal or persistent AF.[4,5] Despite the short anatomical MI length (2–4 cm), achieving BDB across the MI is technically challenging. Previous studies have shown limited success rates (~70%) in achieving BDB.[6,7] Simple endocardial MI ablation may be insufficient for creation of BDB. Up to 70% of patients require additional ablation within the distal coronary sinus (CS) to achieve conduction block across the MI.[4] In some patients, elimination of the epicardial connection through the ligament of Marshall may be required.[8–11] As an alternative strategy to MI ablation, anterior line ablation has been introduced, but advantages of this new approach remain controversial.

We report our experience of MI ablation using different ablation procedures and their clinical outcomes. In this paper, we use the term "MI block" to indicate block across the lateral mitral annular region and use the term "PM block (PMB)" to indicate block either in the MI or in the anterior line.

2. Methods

2.1. Study population and design

We retrospectively enrolled patients who had undergone MI ablation during catheter ablation of AF or atypical AFL using

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3-dimensional (3D) electroanatomical mapping systems (Carto 3; Biosense Webster, Baldwin Park, CA or EnSite NavX; St. Jude Medical, MI) from January 2010 to May 2015. We analyzed the ablation procedures for achieving MI block and clinical outcomes after the procedures. AF was classified according to the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society 2012 Consensus Statement on Catheter and Surgical Ablation of AF.[12] We excluded patients who had previously undergone Maze operation or MI ablation.

The primary endpoint was defined as the achievement of successful BDB across the MI. The MI was considered bidirectionally blocked when the CS electrograms showed a proximal-to-distal activation sequence during LA appendage (LAA) pacing, and the interval of stimulation to the LAA electrogram was longer during distal CS pacing than during proximal CS pacing.[4] The secondary endpoint was the recurrence of atrial tachyarrhythmia (AF, AFL, and atrial tachycardia [AT]), defined as any documented episode of atrial tachyarrhythmia on 12-lead electrocardiography or lasting >30 seconds on Holter monitoring with or without antiarrhythmic medications. On the basis of the guidelines, no episode within the first 3-month blanking period after ablation was counted.[12] The ethical review board at our institution (Asan Medical Center) approved this retrospective study and waived the requirement for informed consent (Approval number: 2015–1159). The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in a priori approval by the institution's human research committee.

2.2. PV isolation

All patients took oral anticoagulation with a vitamin K antagonist or non-vitamin K oral antagonists for ≥3 weeks before the AF catheter ablation. Transesophageal echocardiography was performed in all patients to confirm the absence of thrombus in the LA before the procedure. A duo-decapolar catheter (St. Jude Medical) was positioned in the CS and right atrium for pacing and recording. Activated clotting time was maintained within 300 to 350 seconds by bolus infusion of heparin. After dual transseptal catheterizations, 3D electroanatomical maps of the LA and PVs were reconstructed using a nonfluoroscopic navigation system (Carto 3; Biosense Webster or EnSite NavX; St. Jude Medical). Fast anatomical maps were acquired during AF or sinus rhythm using respiratory gating and an ablation catheter or a 20-pole circular mapping catheter (LASSO; Biosense Webster). We used image integration of the electroanatomical map with the pre-acquired computed tomographic data according to the operator's preference. RF pulses were delivered using a 3.5-mm Navistar Thermocool SF (Biosense Webster) in the Carto 3 system and a 4-mm Therapy Cool Flex Bidirectional Ablation Catheter (St. Jude Medical) in the EnSite NavX system. RF power was set between 30 to 35W around the PV antrum, carina, and ridge, and was reduced to 25 W in the posterior LA near the esophagus. The catheter tip was irrigated using saline at a flow rate of 2 mL/min during mapping and 10 to 17 mL/min during ablation. The lesions around the PVs were created by sequential point-by-point or continuous application of RF energy. Resumption of LA to PV conduction was re-checked 30 minutes after ablation. Additional substrate modification was performed at the discretion of the operator.

2.3. RF ablation for achieving peri-mitral (PM) block

MI ablation was performed when PM AFL was induced by atrial pacing or intrinsic AF was converted into PM AFL during catheter ablation of AF. After complete PVI, endocardial MI linear ablation was tried along the shortest imaginary line between the left inferior PV to the posterolateral MI (Fig. 1A). In the majority of failed cases of endocardial MI ablation, additional ablation within the distal CS was performed (Fig. 1B); when it also failed to achieve conduction block, a new separate MI ablation (double MI lines, Fig. 1C), anterior line (Fig. 1D), or vein of Marshall (VOM) ablation (Fig. 2) was performed in selected patients at the operator's discretion. The new separate MI line ablation was tried ≥1-cm apart from the previous MI line connecting the left inferior PV to the lateral or posterolateral MI (Fig. 1C). RF power was set at 20 to 25 W (temperature limit: 43°C) during the CS ablation and at 30 to 35 W during the MI endocardial ablation.

For RF ablation targeting the VOM, we performed modified CS venography as Yamada et al. suggested.[13] We have previously reported the methods and outcomes of VOM ablation.[14] Briefly, contrast dye was injected manually through the external irrigation lumen with a 5.0-mL syringe and without balloon occlusion after placing an external irrigated ablation catheter in the mid-CS (mitral annulus in the 4–5 o'clock direction) in left anterior oblique projection. If the VOM was visualized, the irrigation catheter was introduced into the ostium of the VOM and selective venography was performed in the same manner (Fig. 2A). If the epicardial ablation around the VOM ostium did not achieve MI block, the endocardial aspect facing the 3D-marked epicardial VOM ostium was targeted (Fig. 2B); if it was ineffective, linear endocardial ablation was tried from the VOM ostium to the left interior PV ridge until MI block was achieved. Coronary angiography was not performed in this study because acute coronary complication was not suspected during or after the procedure.

Anterior line ablation was performed in some failed cases of MI ablation by deploying RF lesions from the anterolateral mitral annulus in the 12 to 1 o'clock direction (in the left anterior oblique 40° view) to the roof line (Fig. 1D).[15] RF power was set at 30 to 35 W during the ablation.

2.4. Statistical analysis

As this was a retrospective study, a sample size calculation was not performed. Continuous variables are presented as the mean ± standard deviation. Student t test was used for variables with normal distributions. Categorical variables are presented as frequencies (percentage) and were analyzed using the Chi-square test. A P value of <.05 was considered statistically significant. All analyses were performed using SPSS (IBM SPSS Statistics, Version 20, NY). Kaplan–Meier survival analysis was used to compare the recurrence of atrial tachyarrhythmia. A multivariable Cox regression model was used to assess the independent predictors for recurrence of atrial tachyarrhythmia after checking for proportional hazard assumption ($P=.26$). The variables of age, sex, body mass index (BMI), persistent AF, LA diameter, ejection fraction, PMB success, redo procedure, hypertension, and diabetes were included in this model.

3. Results

3.1. Study population and baseline characteristics

From January 2010 to May 2015, 738 patients received catheter ablation for AF or atypical flutter with 3D electroanatomical

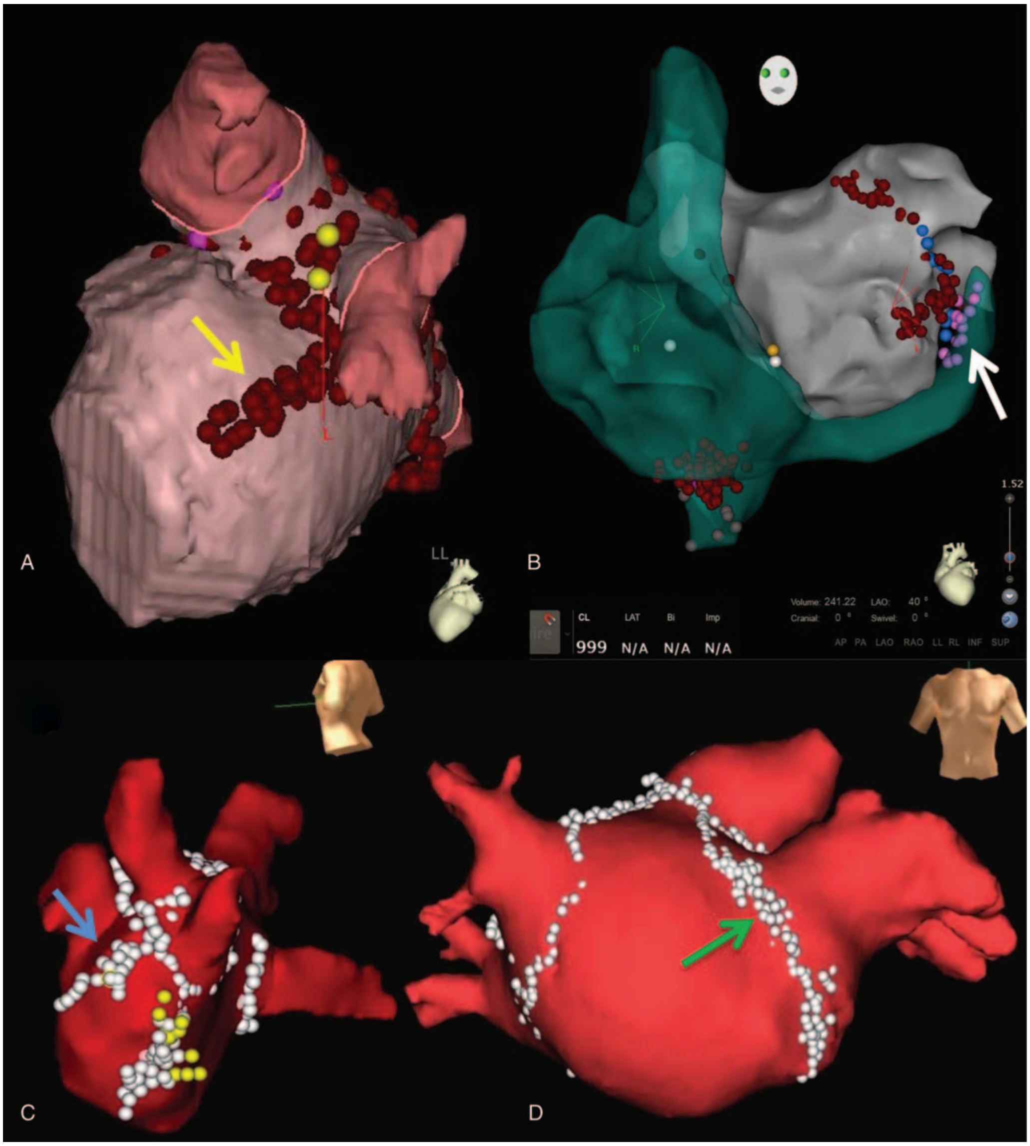

Figure 1. Variable ablation lesion sets for MI block; A: Simple endocardial MI ablation (yellow arrow), B: additional ablation (purple dots) within distal CS (white arrow), C: new separate endocardial MI ablations (blue arrow), Yellow balls indicate ablation points inside the CS, D: anterior line (green arrow) connecting from the roof line to the mitral annulus. Yellow balls indicate ablation points inside the CS. CS = coronary sinus, MI = mitral isthmus.

mapping. MI ablation had been tried in 258 patients. After exclusion of 9 patients who had previously undergone Maze operation and 13 patients who had undergone redo MI ablation, we finally enrolled 236 patients for analysis. The flow chart for selection of the study population is shown in Figure 3.

3.2. Ablation strategies for achieving perimitral block

Among the 236 patients in whom MI linear ablation was tried, single endocardial MI line with or without distal CS ablation accomplished BDB in only 129 (54.7%) patients (Fig. 4). Distal CS ablation was necessary in 94 of 129 patients to achieve a bidirectional MI block. Further ablation by creating a new separate MI line (n = 25), ablation targeting the VOM (n = 19) or anterior line ablation (n = 23) were tried in some of the remaining patients. The success rate of MI block was 52.0% (13/25) with a new MI line and 68.4% (13/19) with ablation targeting the VOM. Overall, a successful BDB across the MI was achieved in 155 (65.7%) patients. The baseline characteristics were similar between the patients with and without successful MI block. The patients with successful MI block had significantly smaller LA size than those with failed MI block (42.2 ± 6.0 mm vs 43.9 ± 5.5 mm, respectively; $P = .04$). The RF delivery time for MI block was significantly longer in the patients with failed MI block than in those with successful MI block (31.7 ± 16.1 min vs 22.6 ± 12.7 min, respectively; $P < .001$). Details of the baseline characteristics are presented in Table 1.

The success rate of the additional anterior line was 52.2% (12/23). Finally, 155 patients achieved MI block, and 12 patients achieved anterior line block. Overall, PMB was achieved in 70.8% (167/236) of the patients. The procedural details for PMB are shown in Figure 4.

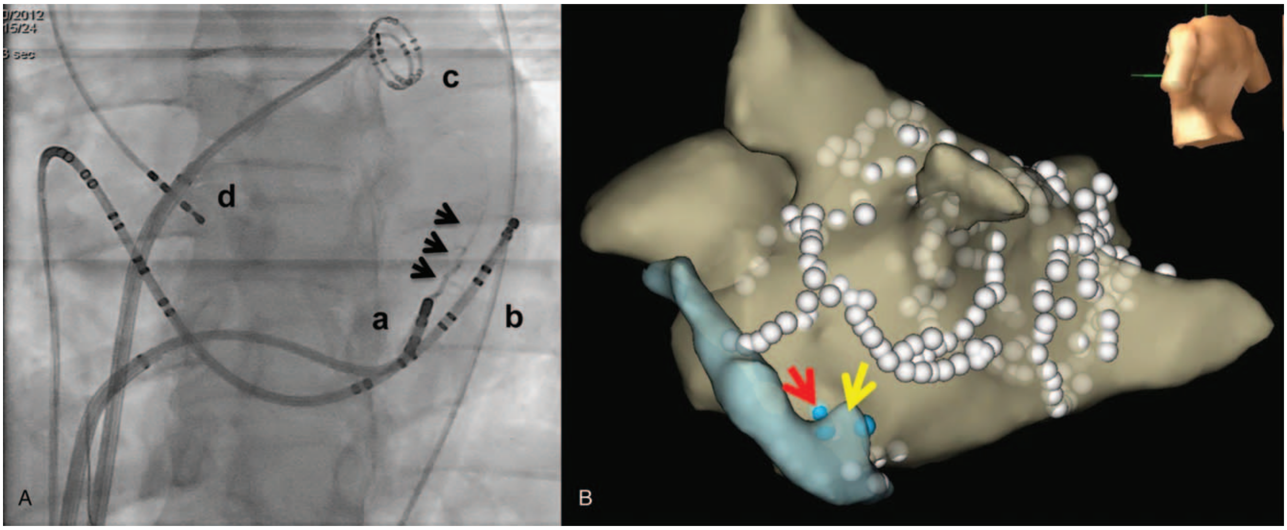

Figure 2. Left panel (A): Modified technique of vein of Marshall (VOM, arrows) venography using an irrigated catheter (left anterior oblique 40° view). Contrast dye was injected through the irrigated-tip ablation catheter. a: a 7-Fr CoolFlex (M curve) 4-mm-tip irrigation catheter was engaged in the ostium of the VOM. b: a 7-Fr Duo-decapolar deflectable catheter was placed in the right atrium and coronary sinus. c: a 7-Fr circular duo-decapolar mapping catheter (Lasso) in the left superior pulmonary vein. d: a 5-Fr reference catheter in the right coronary cusp. Right panel (B): The endocardial ablation points (white dots) are shown on a shell of the left atrium, CS, and stump of the VOM (yellow arrow), which were constructed using a 3-dimensional electroanatomical mapping system (EnSite, NavX). Blue balls at the VOM stump (yellow arrow) indicate the final radiofrequency application site (within CS). The red arrow indicates the ablation site where the mitral isthmus block was achieved. CS = coronary sinus, VOM = vein of Marshall.

3.3. Clinical outcomes

The median follow-up period was 538 days (interquartile range [IR]: 176–1278 days) in patients with failed PMB and 587 days (IR: 193–1108 days) in the patients with successful PMB. The incidences of atrial tachyarrhythmia between the patients with PMB and those without PMB were not significantly different (32.9% vs 42.0%, respectively; $P = .18$). Kaplan–Meier survival analysis for the recurrence of atrial tachyarrhythmia showed no significant difference between the 2 groups (Log-rank, $P = .25$, Fig. 5). In multivariable Cox regression analysis, age (hazard ratio [HR]: 1.03, 95% confidence interval [CI]: 1.01–1.06, $P = .003$) and EF (HR: 0.94, 95% CI: 0.92–0.96, $P < .001$) were significantly associated with recurrence of atrial tachyarrhythmia (Table 2). However, achievement of PMB was not associated with recurrence of atrial tachyarrhythmia (HR: 0.70, 95% CI: 0.43–1.12, $P = .13$).

A redo MI ablation procedure was performed in 15 patients (11 patients with previously successful MI block, 4 patients with failed MI block) during the follow-up. Reconnection of MI was observed in 9 (81.8%) patients with previously successful MI block. Redo ablation of the MI was tried, and MI block was achieved in 7 (77.8%) patients. Both endocardial MI and distal CS ablations were required to achieve BDB across the MI in 5 patients, and the remaining 2 patients eventually needed new MI line ablation to achieve MI block. On the other hand, redo MI ablations were also tried in 4 patients with previously failed MI block. However, only 1 (25%) patient achieved MI block with endocardia MI and distal CS ablation.

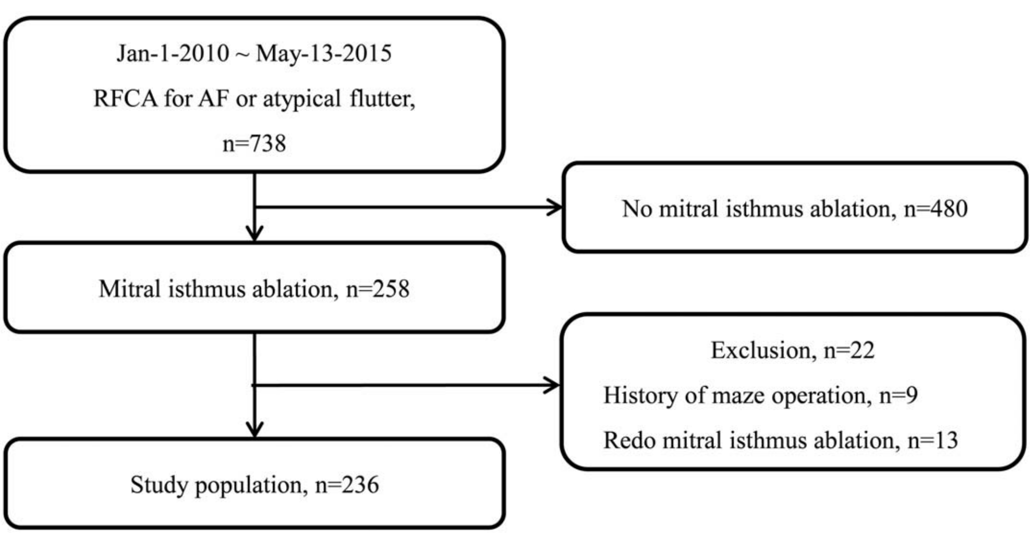

Figure 3. Flow chart of the study population selection process. AF = atrial fibrillation, RFCA = radiofrequency catheter ablation.

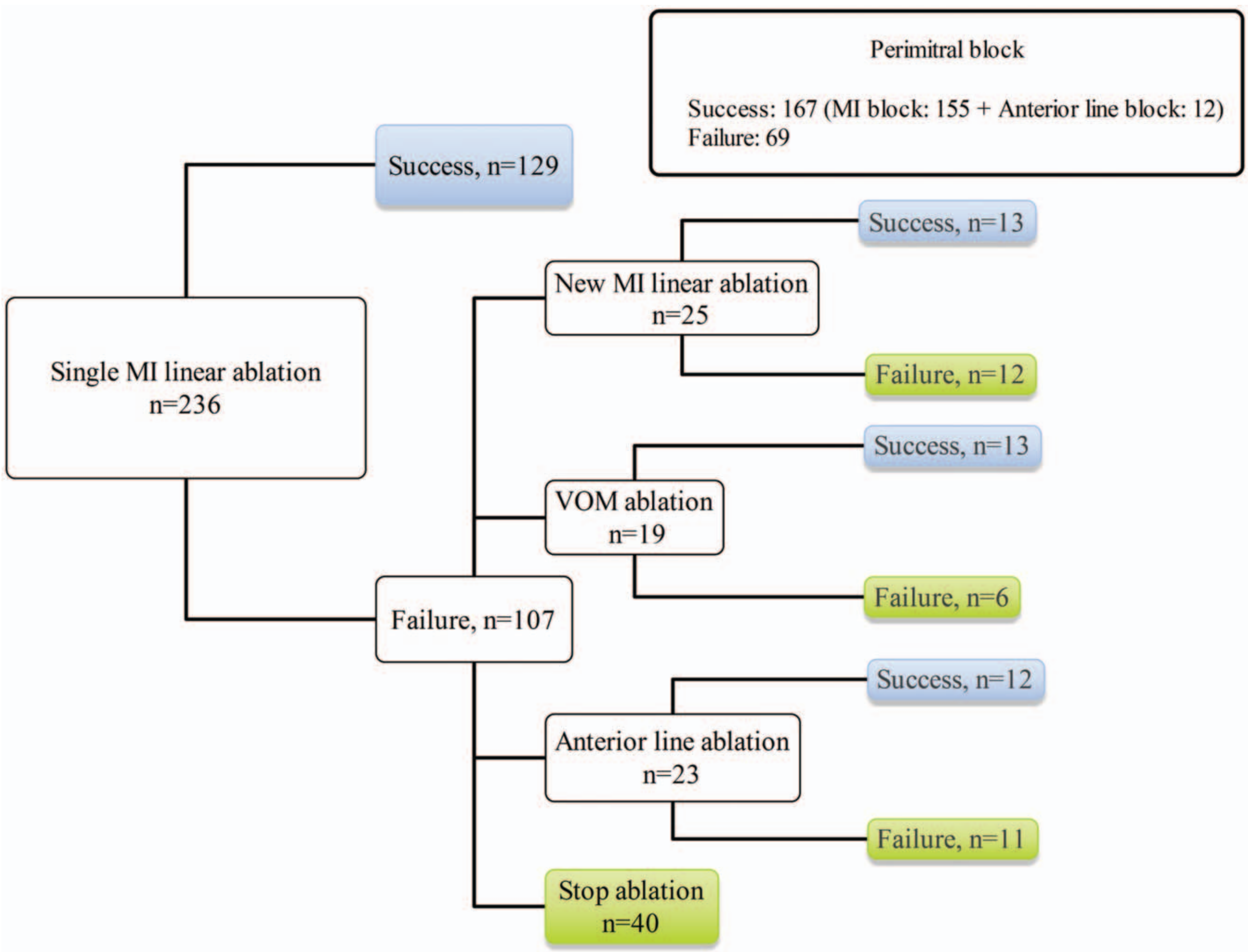

Figure 4. Flow chart of the ablation process for achieving perimitral block in the study population. CS=coronary sinus, MI=mitral isthmus, VOM=vein of Marshall.

Table 1

Baseline characteristics of the study population.

	MI block failure (n=81)	MI block success (n=155)	*P* value
Age	56.9±11.1	57.3±10.9	.81
Male	21 (25.9)	54 (34.8)	.16
BMI, kg/m^2	24.9±1.3	24.8±2.8	.89
Persistent AF	38 (46.9)	94 (60.6)	.04
Redo-ablation	9 (11.1)	20 (12.9)	.69
Past History			
Heart failure	7 (8.6)	23 (14.8)	.18
Hypertension	33 (40.7)	62 (40.0)	.91
Diabetes	7 (8.6)	20 (12.9)	.33
Stroke	5 (6.2)	20 (12.9)	.11
Vascular disease	7 (8.6)	8 (5.2)	.30
CHA_2DS_2VASc	1.4±1.3	1.6±1.4	.22
Hb, g/dL	14.1±1.6	14.2±1.5	.69
Cr, mg/dL	1.1±1.0	1.0±0.5	.16
Ejection fraction, %	57.4±8.8	56.6±8.6	.53
LA size, mm	43.9±5.5	42.2±6.0	.04
Total RFA duration, min	31.7±16.1	22.6±12.7	<.001
Endocardia MI	27.3±14.3	18.3±11.5	<.001
CS (+ VOM)	7.5±7.0	5.7±4.9	.11

Values are expressed as n(%) or the mean±SD. AF=atrial fibrillation, BMI=body mass index, Cr=creatinine, CS=coronary sinus, Hb=hemoglobin, LA=left atrium, MI=mitral isthmus, RFA=radiofrequency ablation, VOM=vein of Marshall.

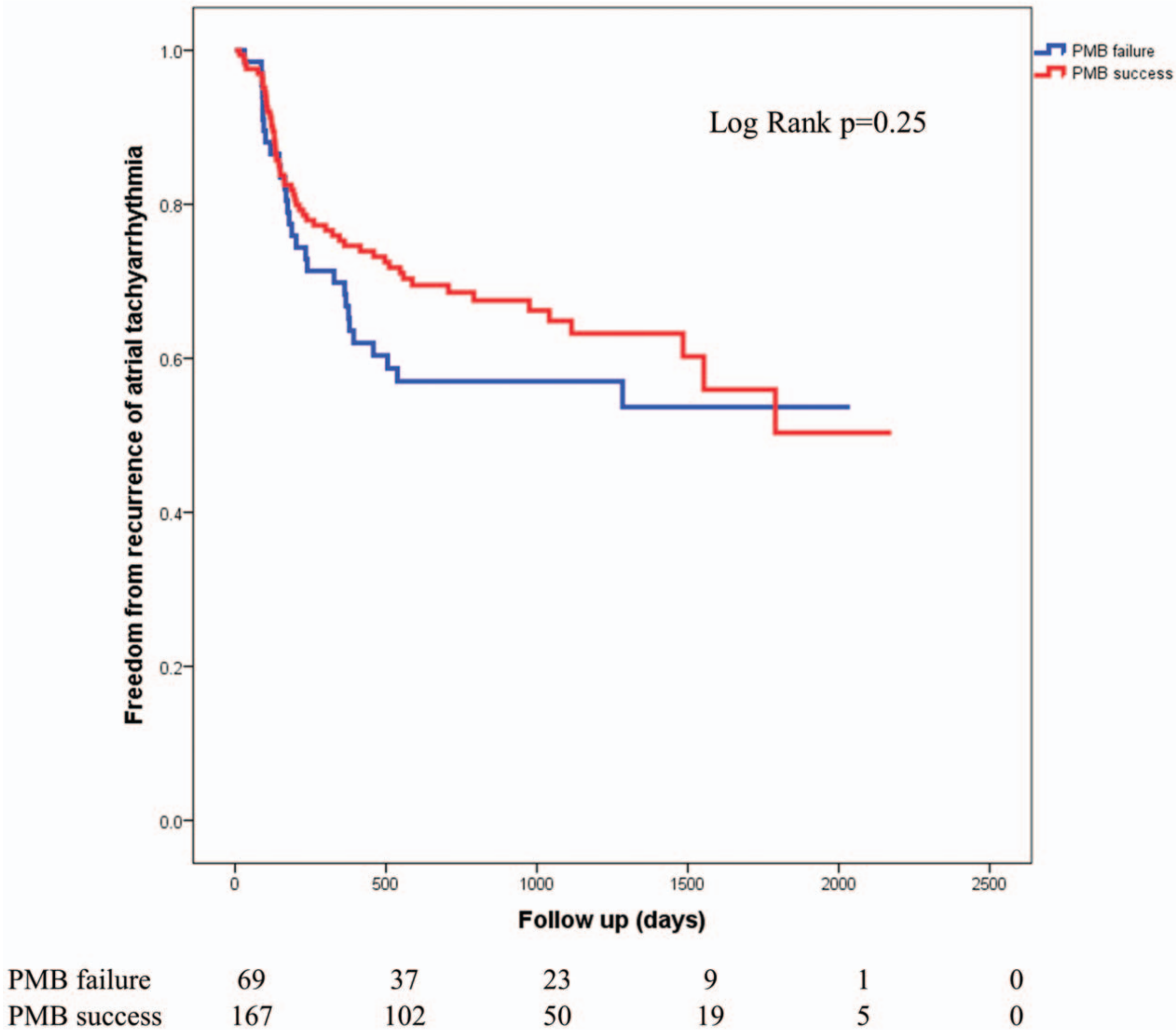

Figure 5. Kaplan–Meier curves for recurrence of atrial tachyarrhythmia according to the results of PMB. The term PMB indicates block either in the mitral isthmus or in the anterior line. PMB=perimitral block.

3.4. Complications

Cardiac tamponade occurred in 10 (4.2%) patients during the entire procedure. All patients were stabilized with immediate pericardiocentesis and supportive care without surgery. Stroke occurred in 1 (0.4%) patient who had an embolic stroke in the cerebellum 1 day after the procedure but experienced a full neurological recovery without sequelae.

Table 2

Multivariable analysis for recurrence of atrial tachyarrhythmias.

	Hazard ratio	95% CI interval	*P* value
Age	1.03	1.01–1.06	.005
Female	1.17	0.72–1.90	.54
BMI, kg/m^2	1.06	0.97–1.15	.21
Persistent AF	1.07	0.66–1.73	.78
LA size, mm	0.98	0.94–1.03	.45
Ejection fraction, %	0.94	0.92–0.96	<.001
PMB success	0.70	0.43–1.12	.13
Redo procedure	0.73	0.35–1.55	.42
Hypertension	0.94	0.56–1.56	.80
Diabetes	0.99	0.48–2.06	.98

AF=atrial fibrillation, BMI=body mass index, CI=confidence interval, LA=left atrium, PMB=perimitral block.

4. Discussion

We described our experience using different ablation strategies to achieve MI block or PMB and presented the outcomes. The main findings of our study were as follows:

1) Creation of the BDB across the MI is difficult to achieve; the success rate of MI conduction block was 65.7% (155/236), consistent with previous studies (70%).[6,7]
2) Additional RF applications, including distal CS ablation, double MI line, VOM ablation, or anterior line, improved the success rate of MI block or PMB.
3) The benefits of PMB were not clear in terms of recurrence of atrial tachyarrhythmia in this retrospective study.

Some anatomical obstacles for MI block have been previously suggested. Anatomical features, including myocardial thickness, presence of recesses or fold, cooling effect of adjacent vessels (left circumflex artery or CS), and presence of epicardial CS connection over MI, might contribute to the failure of MI conduction block.[9,16–18] Making a new separate MI line or anterior line may be a good option if the previous ablation line was located on the recesses or fold. Ablation targeting the distal CS or VOM may be useful for elimination of epicardial conduction over the MI. And these methods may provide incremental benefits by providing successful PMB. A prospective study evaluating the long-term efficacy of these additional lesions is needed.

Extensive ablation to achieve MI block can cause serious complications, including cardiac tamponade, circumflex artery occlusion, and atrio-esophageal fistula.[4,19,20] Increasing the RF power and ablation duration should be avoided because of the increased risk of complications in difficult cases of achieving MI block. Fortunately, left circumflex artery occlusion or atrio-esophageal fistula was not observed in our study population. Cardiac tamponade occurred in 4.2% of the patients. Previous studies regarding MI ablation have reported the incidence of cardiac tamponade as 0.8% to 8%.[4,21,22] Although different ablation catheters and RF power were used, we believe our results are consistent with previous results.

Both MI and anterior line ablation are effective in treating macro-reentrant PM AFL. Superiority of the anterior line has been suggested, but the advantage of MI ablation over the anterior line has also been discussed. First, the MI is the area of the latest atrial activation during sinus rhythm. Thus, linear ablation in this area does not alter the LA activation pattern.[4] However, anterior line ablation, by transecting the transatrial conduction through the LA, can change the propagation pattern with the late activation of LAA during sinus rhythm.[23] This change may be related to hemodynamic alteration (simultaneous contraction of the LAA and left ventricle) and increased risk of stroke.[23] Especially, careful considerations are required when failed MI ablation is switched to anterior line ablation because the combination of these 2 procedures can cause LAA isolation and thrombus formation despite oral anticoagulation medications.[24] Although LAA isolation was not observed in the present study, substantial delays of LAA activation even after inscriptions of the QRS complex were observed in 13.0% (3/23) of the patients who underwent anterior line ablation after failed MI block. They all subsequently showed no measurable late diastolic or mitral A wave during sinus rhythm in follow-up echocardiography (Fig. 6). Second, MI is anatomically shorter (2–4 cm). Thus, theoretically, MI ablation carries less chance of leaving a conduction gap than does anterior line ablation.[4] This conduction gap is well known to be proarrhythmogenic of re-entrant arrhythmia.[25]

The VOM is a remnant structure of the left superior vena cava.[26] Since the proximal and distal portions were connected to the CS myocardial sleeve and left PV, respectively, this epicardial structure can act as a bridge over the MI, making the endocardial MI ablation ineffective. Previously, the benefit of VOM ablation for MI block was suggested in several case reports.[10,27] We performed VOM ablation in a very limited number of patients.

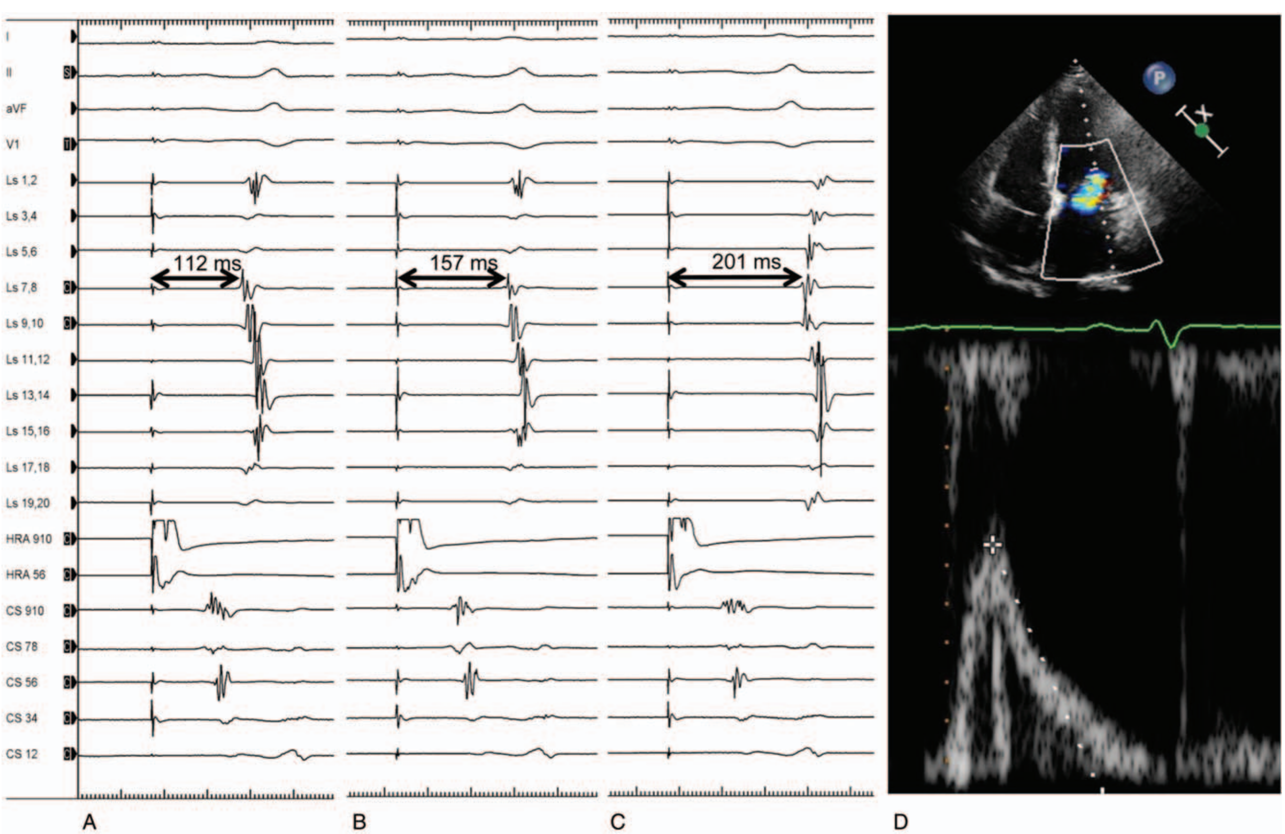

Figure 6. Anterior line ablation after failure of the MI ablation caused significant conduction delay of the LAA. The anterior ablation was performed during high right atrial pacing (HRA 9,10). The lasso catheter was placed in the LAA. At baseline, the stimulus to the earliest LAA potentials was 112 ms (A). However, the interval increased to 157 ms during the anterior ablation (B) and finally increased to 201 ms at the end of ablation (C). LAA activation occurred after onset of the QRS complex after achievement of anterior line block. The follow-up echocardiography did not demonstrate the late diastolic or mitral A wave during sinus rhythm, which suggested a significant intra-atrial conduction delay with ineffective left atrial emptying (D). LAA = left atrial appendage, MI = mitral isthmus.

Thus, the efficacy of VOM ablation for MI block could not be precisely assessed in this study. However, it is meaningful that we demonstrated the benefits of VOM ablation in a relatively large patient cohort.

In the present study, successful PMB was not associated with a lower recurrence rate of atrial tachyarrhythmia. In fact, the benefits of additional substrate modification, including MI ablation after PVI in patients with persistent AF, is controversial.[21] A recent randomized control trial failed to demonstrate the benefits of additional linear lesions or complex fractionated atrial electrogram ablation after PVI.[21] This finding is in contrast to previous reports that have suggested sinus rhythm maintenance benefits of MI ablation, particularly in patients with persistent AF.[4,5,28] Our results appeared to be consistent with the results of a recent multi-center trial, but cautious interpretation is required because our study subjects were not randomized. A future large-scale study is required to clarify this issue.

4.1. Study limitations

This study had several limitations. First, this was a retrospective observational study performed at a single center, so selection bias may have influenced our results. Second, selection of the additional ablation strategy was left to the discretion of the operators, and the relative efficacies of different ablation strategies (double MI line, additional anterior line, or VOM ablation) could not be assessed. Third, extensive monitoring of the recurrence of atrial tachyarrhythmia, such as 7-day Holter monitoring or implantation of a loop recorder, was not performed in our patient cohort. Thus, the recurrence rate of atrial tachyarrhythmia might have been underestimated. Lastly, all procedures including PVI were performed using RF ablation. Thus the results of present study may not be applicable to the patients, treated with cryoballoon that is an another excellent treatment option for paroxysmal and persistent AF.[29,30]

5. Conclusion

Single endocardial MI line with or without distal CS ablation alone was insufficient to achieve MI block. Additional RF applications including double MI line ablation, anterior line ablation, or ablation targeting the VOM improved the MI block and PM block success rate. However, the benefits of PMB for prevention of atrial tachyarrhythmias were not clear in this study. A further large-scale study is required to resolve this issue.

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Writing – original draft: Ji Hyun Lee.
Writing – review & editing: Gi-Byoung Nam.

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