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ORIGINAL ARTICLE
Arrhythmia/Electrophysiology

Epicardial Atrial Mapping Can Predict Elimination of Chronic Atrial Fibrillation After the Box Pulmonary Vein Isolation During Mitral Valve Surgery

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Background: The pulmonary veins (PV) and posterior left atrium (LA) may contribute to the occurrence and maintenance of atrial fibrillation (AF). We evaluated whether simple epicardial electrophysiological mapping can predict elimination of chronic AF after the box PV isolation procedure.

Methods and Results: Using a computerized 48-channel mapping system, we performed intraoperative atrial mapping in 16 patients with chronic AF associated with mitral valve (MV) disease. Patients' ages ranged from 48 to 76 years (mean, 61.4 years). AF duration ranged from 1 to 16 years (mean, 7.5±5.4 years). Simple box PV isolation was performed during the MV operation. Regular and repetitive activation was found in the LA of 12 of 16 patients, and irregular and chaotic activation was found in both atria in 4 of 16 patients; 12 patients with regular and repetitive activation of the LA were treated by box PV isolation and the other 4 patients with irregular and chaotic activation in both atria did not recover sinus rhythm after this procedure. AF-free rate was significantly higher in patients with regular and repetitive activation of the LA ($P<0.01$).

Conclusions: Box PV isolation was effective in the treatment of chronic AF associated with MV disease. Epicardial atrial mapping may predict elimination of AF after the box PV isolation. (*Circ J* 2012; **76:** 852–859)

Key Words: Atrial fibrillation; Electrophysiological study; Isolation; Pulmonary vein; Surgery

Although the pathogenesis of chronic atrial fibrillation (AF) associated with mitral valve (MV) disease is still equivocal, most investigators agree that an increased hemodynamic burden because of inflammation or degeneration of MV can increase tissue fibrosis in the atria, resulting in a non-homogenous distribution of diastolic depolarization potentials, refractory periods, and conduction properties within the atrial muscle.[1,2] Most surgeons subscribe to the multiple reentry theory as the mechanism responsible for AF,[3] which is the basic theory of the Cox maze procedure.[4] The Cox maze procedure was devised as a radical procedure for lone AF, but this procedure was effective for all kinds of AF. The Cox maze procedure and its modifications[5,6] have shown effective results in both short-term and mid-term follow-up. The modified Cox maze procedure using a bipolar radiofrequency device was also devised instead of the cut and sew maze procedure from 2004 onwards.[7]

Our previous study performed on MV disease showed a shortened refractory period for the left atrial wall, and that the simple left atrial procedure was adequate in eliminating the AF associated with isolated mitral disease.[8] We performed the simple left atrial procedure for chronic AF during MV surgery from 1993 to 1998,[9] and reported our mid-term[10] and long-term[11] results. Our initial report[8] augumented AF study and connected the discovery of ectopic foci from pulmonary veins (PV) that had been reported by Haissaguerre et al.[12] We then hypothesized that chronic AF also occurred via ectopic foci from the PV and was maintained by activation of the posterior left atrium (LA) itself. Therefore, from 1999 to 2004 we performed the box PV isolation procedure for chronic AF associated with solitary MV disease without any ablation lines on the right atrium (RA) and MV annulus.[13] The purpose of this study was to examine whether or not intraoperative epicardial atrial mapping might predict elimination of chronic AF after the simple surgical box PV isolation procedure.

Methods

Informed Consent and Ethics Approval

Informed consent for this surgery and the postoperative follow-up study was given by every patient according to the manual of informed consent of the Hiroshima University Hospital. The Ethics Committee of Hiroshima University Hospital approved this clinical study in every patient. There was no conflict with

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Table 1. Baseline Profiles of 16 Patients

No.	Age (years)	Sex	Valve	AF duration (years)	LAD	EF	Complications	Results
1	53	F	MVR	14	56	52	Hyperthyroidism	AF
2	61	F	MVSR	4	50	58	DM	SR
3	53	F	MVSR	8	51	54	–	SR
4	62	M	MVR	16	60	44	PVC	AF
5	61	F	MVSR	5	52	63	–	SR
6	48	M	MVR	6	56	65	Hyperthyroidism	SR
7	62	F	MVR	5	62	49	Dialysis, pace SR	
8	76	F	MVSR	10	67	44	–	AF
9	62	M	MVR	9	61	31	DM, thrombus	AF
10	73	F	MVR	6	48	52	Cerebral embolism	SR
11	70	M	MVR	1	45	64	–	SR
12	64	M	MVS	7	50	58	–	SR
13	60	M	MVR	8	56	52	–	SR
14	61	F	MVSR	9	62	47	–	SR
15	59	M	MVR	4	55	61	–	SR
16	57	F	MVSR	8	60	46	Thrombus	SR
	61.4±7.2			7.5±3.7	55.4±6.2	52.7±9.2		

AF, atrial fibrillation; LAD, left atrial diameter; EF, ejection fraction; MVR, mitral valve regurgitation; MVSR, mitral valve stenosis and regurgitation; DM, diabetes mellitus; SR, sinus rhythm; PVC, premature ventricular contraction; MVS, mitral valve stenosis.

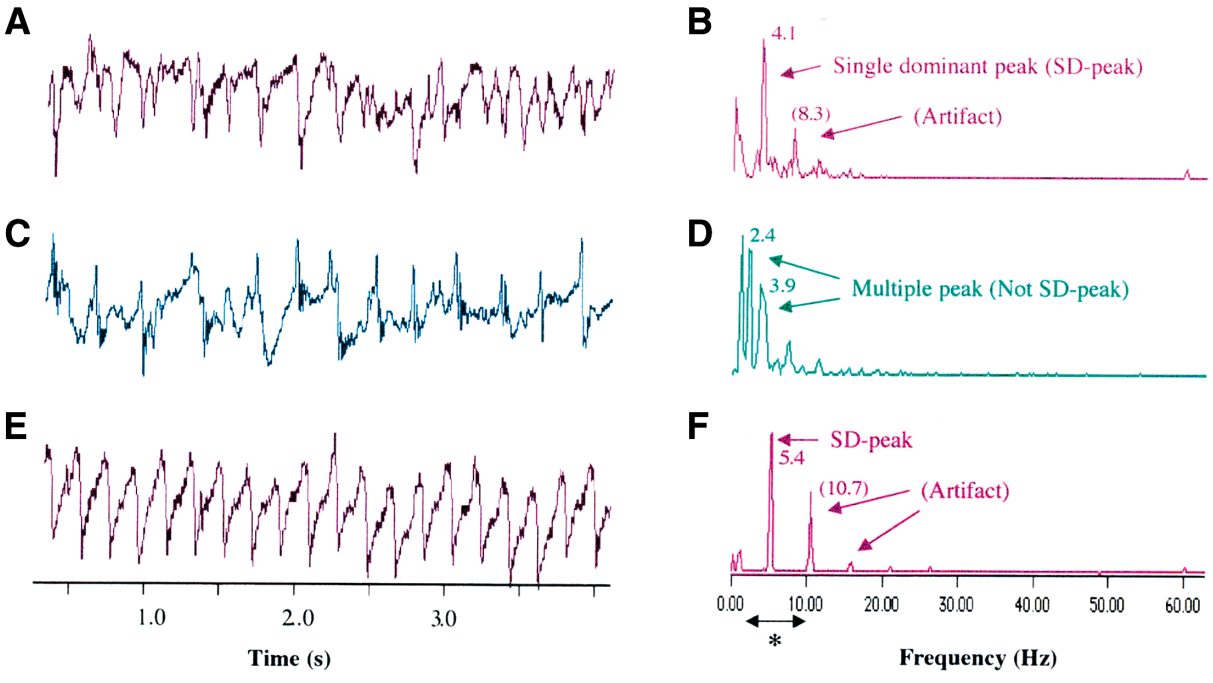

Figure 1. Bipolar electrograms with corresponding analysis data. (**Left**) Bipolar electrograms of patients 1, 2 and 3. (**Right**) Corresponding frequency spectra produced by fast-Fourier transform (FFT). (**B**,**E**) Examples of single dominant peaks (SD-peak) (patients 2 and 3); (**D**) multiple peaks (patient no. 1). We defined a single dominant peak as regular and repetitive activation (**B**,**E**: patients 2 and 3) and multiple peaks as irregular and chaotic activation (**D**: patient no. 1). *Range for analysis (1–10 Hz).

any medical company.

Subjects

From February 1999 to April 2001, 16 patients with MV disease and chronic AF underwent the box PV isolation procedure in patients with chronic AF associated with solitary MV disease. The patients consisted of 7 men and 9 women, and ranged in age from 48 to 76 years (mean, 61.4 years). AF duration ranged from 1 to 16 years (mean, 7.4±5.4 years). **Table 1** shows the profiles of these patients. Chronic AF was diag-

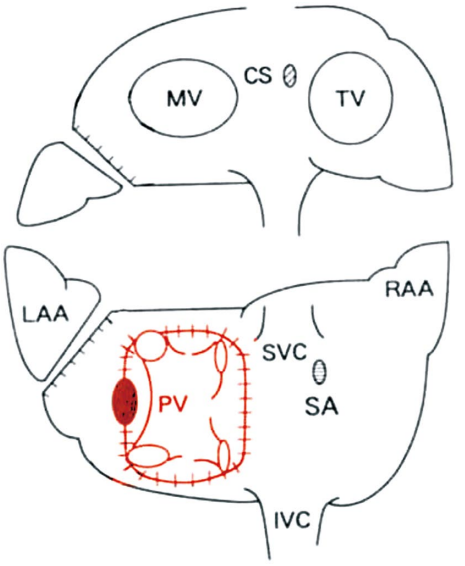

Figure 2. Schema of the box pulmonary vein isolation procedure. A left-vertical atriotomy is extended to the left margin of the left pulmonary veins. After excision and closure of the left atrial appendage, cryoablation is delivered at –60°C for 3 min to the posterior wall of the left atrium. The cryoablation is directed towards the incision edges between the upper and lower left pulmonary veins. (Black area, cryoablation; dashed lines and hatched areas, incision and suture line). CS, coronary sinus; IVC, inferior vena cava; LAA, left atrial appendage; MV, mitral valve; PVs, pulmonary veins; RAA, right atrial appendage; SA, sinus node; SVC, superior vena cava; TV, tricuspid valve.

nosed by ECG or Holter ECG by their medical records. There were no patients with paroxysmal AF.

Intraoperative Epicardial Atrial Mapping

Before the institution of cardiopulmonary bypass, intraoperative atrial mapping was performed with 2 card-type electrodes and a Fukuda electronic mapping system (Fukuda model HPM-7100, Tokyo, Japan). The card-type electrode had 24 small, bipolar electrodes of 2-mm diameter each, mounted in 4 rows of 6 on a flexible plastic rectangular sheet (33×50 mm). The 2 card-type electrodes were attached to the LA epicardial surface (between the LA appendage and the left PV) and the RA epicardial surface. Atrial mapping was then performed for both atria, and bipolar epicardial electrograms were recorded continuously on diskette for off-line signal processing by a computerized mapping system. All the differential amplifiers had a frequency response of 10–100 Hz. A computer stored and digitized all of date, and displayed the wave forms. Atrial epicardial wave forms for a 50-ms window were produced automatically, and were displayed sequentially. After all the atrial epicardial electrograms had been recorded for 40 s, the local epicardial cycle length (CL) was calculated by measuring the interval between the steepest deflection of each activation point in a 10-s window. The AFCL was averaged to obtain the mean AFCL (MAFCL). The epicardial activation wave form for both atria was then divided into 2 types: irregular and chaotic activation, and regular and repetitive activation. All the atrial electrophysiological studies were performed in the operating room.

Dominant Peak Detection

The periodicity of atrial activation was examined using spectral analysis at 48 points. Three examples are shown in **Figure 1**. Bipolar electrograms from each epicardial sampling point and the corresponding power spectrum, using a fast-Fourier transform (FFT), are shown. Because the amplitude of ECGs varied among sampling points and cases, the electrogram was arbitrarily scaled along the ordinate to conveniently present 3 examples. Similarity in FFT, the power axes are not the same because the total power varied according to the amplitude of the bipolar electrogram. Although the bipolar electrogram of **Figure 1A** apparently shows irregular electrical activity, the FFT (**Figure 1B**) indicates a single narrow-band peak at 4.1 Hz within the analysis range. Note the peak at 8.3 Hz (twice as high as 4.1 Hz), which is a double harmonic frequency (artifact). We diagnosed this electrogram as regular and repetitive activation (patient no. 2). The bipolar electrogram of **Figure 1C** shows irregular and chaotic activation. **Figure 1D** (FFT of **Figure 1C**) shows multiple peak formation. Although 2 narrow-band peaks are apparent, the frequency of the second peak (3.9 Hz) is not double that of the maximum peak. We diagnosed this electrogram as irregular and chaotic activation (patient no. 1). The bipolar electrogram of **Figure 1E** demonstrates regular and repetitive atrial activation, and the FFT (**Figure 1F**) shows a sharp, discrete peak. We diagnosed this bipolar electrogram as typical regular and repetitive activation (patient no. 3).

Surgical Procedure

The operations were performed with the use of cardiopulmonary bypass with mild hypothermia (34°C) and cold blood cardioplegia. Before aortic cross-clamping, distal coronary arterial anastomoses were performed during an on-pump beating heart in cases that required coronary artery bypass grafting. A proximal anastomosis using a saphenous vein graft was performed during re-warming. After aortic cross-clamping and infusion of blood cardioplegia, a vertical left atriotomy was extended to the left margin of the left PV. The LA appendage was excised and closed from the inside. Cryoablation (–60°C for 3 min,) with a T-shaped cryoprobe (20 mm in length and 8 mm in width, Tonokura, Tokyo) was applied towards the posterior wall of the LA between the upper and lower incision ridges (**Figure 2**). After the isolation of all PV with surgical incisions and cryoablation, the MV procedure was completed. We did not perform ablation towards the MV annulus. No further atriotomy was performed on the atrial septum or RA for elimination of chronic AF. After completion of these AF procedures, the left atriotomy was closed with a running suture. All patients in this series were operated on by the same surgical team.

Data Acquisition and Statistical Analysis

The disappearance of the AF was defined as no detectable AF at discharge, and again at 6 months after the operation. All values are expressed as means±standard deviation. All collected data were entered into a database. Continuous variables were then compared using the nonparametric Mann-Whitney U test. The proportions were compared with Fisher's exact test. A P value less than 0.05 was considered to be statistically significant. Time-dependent morbidity was tabulated univariately by a Kaplan-Meier life-table with the endpoint of recurrence of sustained AF diagnosed by ECG. The statistical analysis was performed using the StatView J-4.5 software package (Abacus Concepts, Berkeley, CA, USA).

Table 2. Comparison of Preoperative and Intraoperative Variables

	Non-AF Group	AF Group	P value
Preoperative factors			
M/F	5/7	2/2	0.712
Age at surgery (years)	60.8±8.4	63.2±11.4	0.642
Duration of AF (years)	5.4±3.6	12.3±3.2	0.012
Amplitude of f-wave at lead V_1 (mV)	0.18±0.09	0.12±0.07	0.086
Cardiothoracic ratio (%)	56.2±8.2	61.8±4.7	0.078
Echocardiography			
Ejection fraction (%)	55.8±9.2	42.8±8.3	0.087
Left atrial dimensions (mm)	53.9±12.8	61.0±5.2	0.041
Intraoperative factors			
Duration of extracorporeal circulation (min)	110±35	114±38	0.712
Duration of aortic cross-clamping (min)	85±26	90±34	0.494
Associated surgical interventions			
CABG	2	1	0.425
LA thrombectomy	1	1	0.345
Regular and repetitive activations in the LA	12/12	0/4	<0.001

All values are expressed as means±standard deviation or as numbers of patients.
AF, atrial fibrillation; lead V_1, first precordial lead; CABG, coronary artery bypass grafting; LA, left atrium.

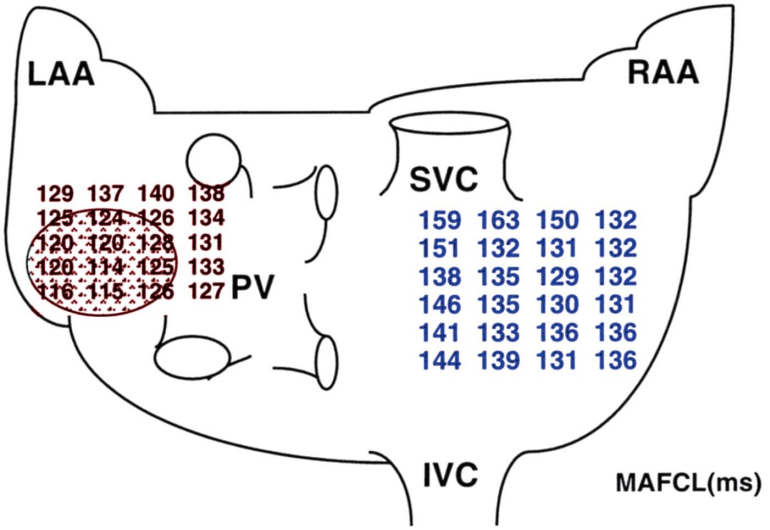

Figure 3. Schema of the distribution of the 48 epicardial electrodes (**Top**) and mean atrial fibrillatory cycle length (MAFCL) of both atria. Distribution of the epicardial electrodes from 1 to 24 in the RA and from 25 to 48 in the LA (**Top**). The MAFCL ranged from 130 to 163 ms in the RA and from 114 to 139 ms in the LA. LA, left atrium; RA, right atrium.

Results

Operative Procedure, Mortality, and Morbidity

The box PV isolation procedure for chronic AF was completed in every patient. The duration of cardiac arrest ranged from 46 to 112 min (mean, 76±35 min), and the cardiopulmonary bypass time from 68 to 148 min (mean, 108±40 min). No patients required postoperative circulatory support, such as intraaortic balloon pumping, and there was no re-exploration for postoperative hemostasis. There was no postoperative mortality. No patient had any severe cerebral thromboembolic complications postoperatively, even those with a recurrence of AF. The results of AF surgery are summarized in **Table 2**.

Epicardial Electrophysiological Mapping

The atrial epicardial electrograms seemed to be regular and repetitive at 5 per 24 (5.0±2.0) points in the LA of 12 of the 16 patients, but were irregular and chaotic at all points in the RA in all 16 patients. Four of 16 cases showed irregular and chaotic electrograms in all points of both atria. The MAFCL ranged from 173 to 319 (mean, 237) ms in the RA, and from 151 to 268 (mean, 184) ms in the LA (**Figure 3**). The shortest AFCL of the LA was observed at the root of the left upper PV in most patients. **Figure 4** shows the lead III ECG, and 8 of 48 bipolar epicardial ECG, recorded from both atria during chronic AF in a 53-year-old woman (patient 3 in **Table 1**). In this patient, a regular and repetitive activation sequence was detected at several points in the LA, in contrast to the irregular and chaotic activation of the RA. This typical activation pattern was observed in 12 of 16 patients, and the chronic AF in these 12 patients was effectively treated by box PV isolation. The other 4 patients showed irregular and chaotic activation in both atria (**Figure 5**, which shows the lead II electrogram and 8 of 48 bipolar electrograms: patient 9 in **Table 1**). These 4 patients did not recover normal sinus rhythm (SR) after surgery.

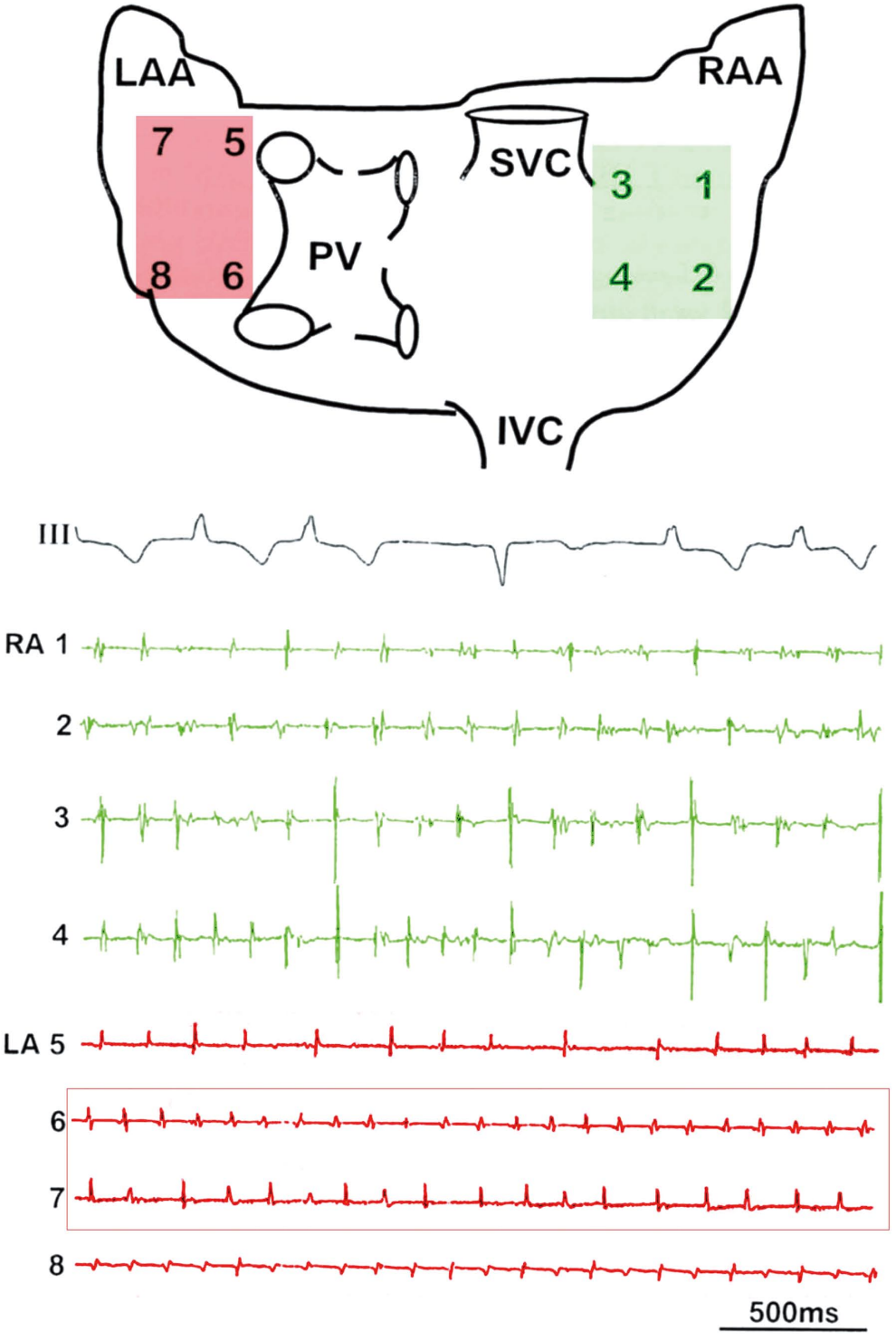

Figure 4. Distribution of the surface electrodes and the surface lead II electrocardiogram and 8 representative bipolar epicardial electrograms in an AF-free case (patient no. 3). The typical 8 electrodes are distributed from 1 to 4 in the RA and from 5 to 8 in the LA. The LA showed regular and repetitive activations (points 5, 6). The RA showed irregular and chaotic activations (points 1, 2, 3, 4). AF, atrial fibrillation; LA, left atrium; RA, right atrium.

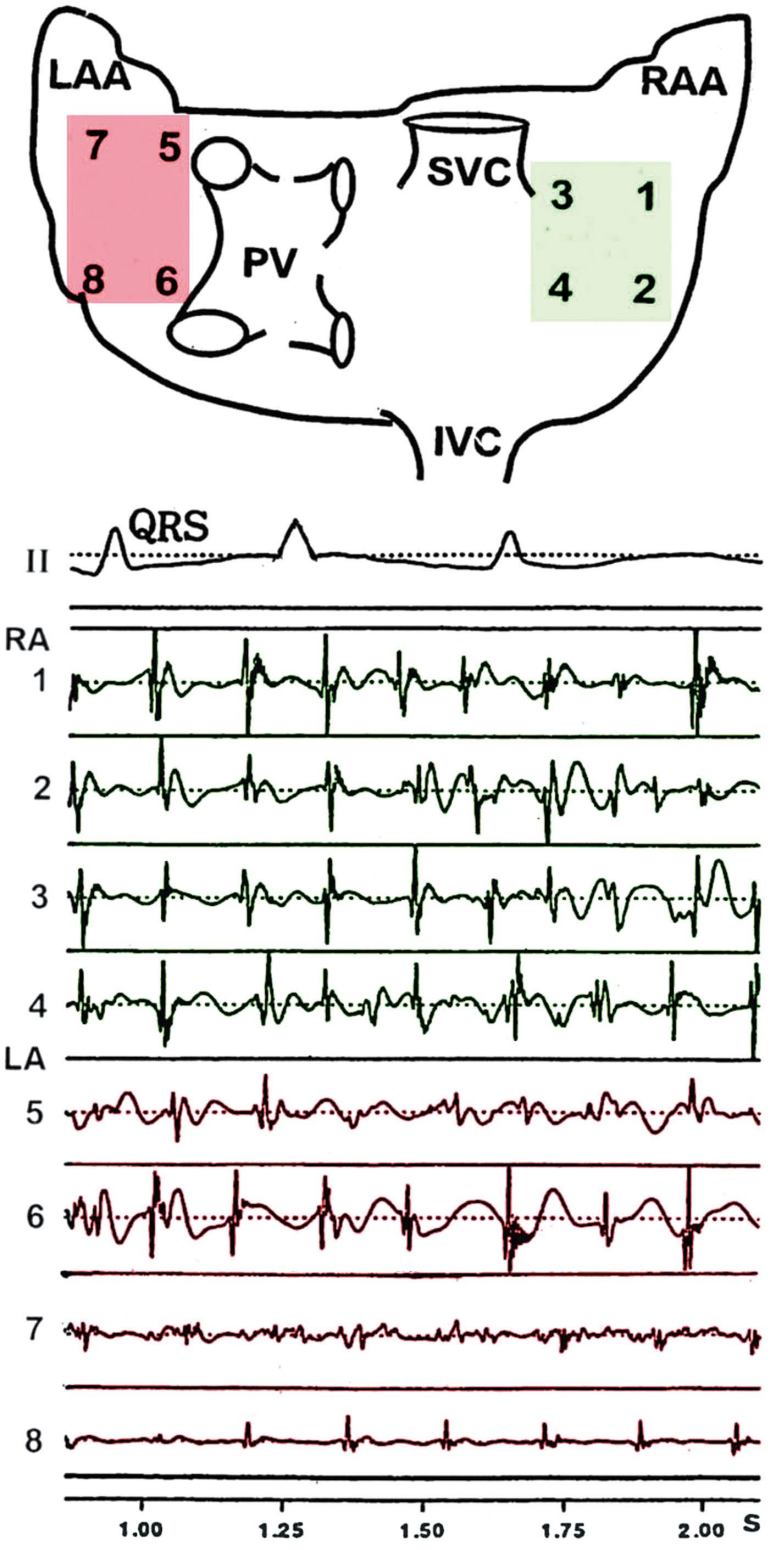

Figure 5. Distribution of the surface electrodes and the surface lead II electrocardiogram and 8 representative bipolar epicardial electrograms in an AF-recurrent case (patient no. 9). The typical 8 electrodes are distributed from 1 to 4 in the RA and from 5 to 8 in the LA. The LA showed irregular and chaotic activations (points 5, 6). The RA also showed irregular and chaotic activations (points 1, 2, 3, 4). AF, atrial fibrillation; LA, left atrium; RA, right atrium.

Postoperative Atrial Arrhythmias and Sinus Node Dysfunction

In 6 of 16 patients (38%) there was transient AF recurrence during the hospital stay, especially the 2nd or 3rd day after operation. These patients required antiarrhythmic drugs (Class Ia) or direct current cardioversion in the intensive care unit or the bet room for restoring SR and could obtain SR. In 2 of 6 AF patients, SR was restored after discharge and they maintained SR during the follow-up period; 4 of 16 patient (25%) showed persistent AF after discharge and were not responsive to direct cardioversion or antiarrhythmic medication during hospital stay; however, 1 of the 4 AF patients recovered SR with antiarrhythmic drugs (Class Ia) at 3 months after opera-

Table 3. Other Postoperative Atrial Arrhythmias in the Non-AF Group

Event	No. of patients
Perioperative recurrent AF	6 (37.5%)
Prophylactic pacemaker implantation for sinus bradycardia	1 (6.3%)*

*Increase heart rate for sinus bradycardia (<50/in) despite no symptoms.
AF, atrial fibrillation.

tion. All patients had a follow-up survey, ranging from 7 years to 11 years (mean follow-up period, 9.2 years) at the out-patient clinic every 6 months. One of the 16 patients died of colon cancer 8 years after AF surgery. The final AF-free rate was 80% (12/15) at the latest follow-up. The AF-free rate in patients with regular and repetitive activation in the LA was significantly higher than that in patient with irregular and chaotic activation of both atria (100%; 12/12 vs. 25%; 1/4, P<0.01). Other atrial tachycardia, such as atrial flutter or LA tachycardia, did not occur in these 12 patients. One of 16 patients (6.3%) underwent prophylactic pacemaker implantation because of sinus bradycardia (<50 beats/min), although she was asymptomatic. A dual-chamber pacemaker was implanted to achieve the appropriate heart rate and atrioventricular sequential contraction was clearly established with atrial kick after pacemaker implantation (Table 3).

Discussion

Chronic AF associated with MV disease often persists despite correct repair of the cardiac defect.[8] The MV operation itself rarely stops the arrhythmia.[14] Our previous data also revealed that the rate of recovery of SR was much higher in those patients who underwent an AF operation than in those who did not (disappearance rate 27% in the control group vs. 86% in the AF operation group at discharge).[9] A high incidence of cerebral infarction was revealed by the J-RHYTHM registry.[15] Antiarrhythmic drugs are effective for paroxysmal AF, but not for persistent AF.[16] Although various concepts involving reentry and ectopic foci have been proposed to explain the mechanism underlying AF,[12] the real mechanism underlying chronic AF associated with MV disease remains unknown. Harada et al reported atrial activation during chronic AF in patients with isolated MV disease, and described a regular and repetitive activation pattern in the LA and an intricate activation pattern in the RA.[17] Our previous study also revealed regular and repetitive activation of the LA in 7 of 11 patients with MV disease.[8] Haissaguerre et al reported the spontaneous initiation of AF by ectopic beats from the PV,[12] and the successful application of radiofrequency ablation at these focal sources. We also observed repetitive activation originating from the left PV during chronic AF with MV disease.[13] Moreover, the shortest AFCL was recorded in the LA in all cases. Morillo et al devised a canine model of sustained AF, which was induced by chronic, rapid atrial pacing. They calculated the AFCL by measuring the interval of the steepest deflection of each monopolar atrial electrogram, and reported that the AFCL represented the refractory time of the atrial contractions and that the AFCL of the LA was shorter than that of the RA in their canine model.[18] We also measured the AFCL by measuring the steepest deflection of each activation using a bipolar electrode (2 mm) and the waves were thought to be as similar as those of monopolar electrodes. We speculate that a shortened refractory period and conduction depression between both atria might play a role in the maintenance of chronic AF associated with isolated MV disease. In this study, we hypothesized that these regular activations might originate from the PV, similar to the activation in cases of paroxysmal AF, and make repetitive regular activations around the PV. Therefore, we estimated the epicardial electrograms and used them to predict AF elimination in this study. Chronic AF was successfully treated in patients who showed regular and repetitive activations in the LA. This clinical observation supports Kalifa's hypothesis[19] that the posterior LA harbors regular, fast, and highly organized activity and gives rise to the most fractionated activity in adjacent locations. Although our mapping could not get all of the epicardial electrograms from both atria and the number of mapping points was small (only 48 points), our data suggest that wave fractionation at boundaries of high-frequency excitation in the posterior LA may be the mechanism of sustaining AF during chronic AF.

We could not differentiate the relation between epicardial atrial electrograms and complex atrial fractionated electrograms (CFAE),[20] which were recorded from the atria during persistent AF. CFAE is defined as electrograms displaying 2 deflections that are fractionated or have a short CL (<120 ms).[19] Work in human electrophysiology has confirmed the dominance of CFAE around the PV in paroxysmal AF.[20] During epicardial atrial mapping, we could not measure CFAE because our mapping points were not situated in PV, the roof of the LA, the coronary sinus or the interatrial groove, where Nademanie et al found CFAE during persistent AF.[20] After isolation of arrhythmogenic PV and posterior LA, the foci of AF and the most fractionated boundary locations might be removed and chronic AF could be eliminated by simple box PV isolation.

There were no cases of MV annulus tachycardia in the SR patients, in whom we did not perform cryoablation towards the MV annulus. A high incidence of atrial tachycardia was reported after widespread LA catheter ablation, which creates a proarrhythmic effect from either incomplete PV isolation or a linear lesion towards the MV annulus.[22] Perimitral reentry can be promoted by an isthmus located between the lateral aspect of an inferior LA lesion and the anterior aspect of the encircling lesion around the left PV.[23] In contrast, surgical box PV isolation can create a definite ablation line around all PV. We can preserve a large and healthy area of atrial myocardium from 3 to 4 cm in width between the left PVs and the MV annulus, which prevents the creation of an isthmus and perimitral reentry.

Study Limitations

The number of patients was too small to clarify the exact relation between epicardial atrial electrograms and elimination of chronic AF. In addition, the number of bipolar epicardial mapping points was very small and limited in positions. However, this study teaches us that simple epicardial atrial mapping may predict the success of box PV isolation for chronic AF. Further epicardial electrophysiological study may elucidate the real mechanism of persistent and chronic AF.

References

1. Ten eick RE, Singer DH. Electrophysiological properties of diseased human atrium. I: Low diastolic potential and altered cellular response to potassium. *Circ Res* 1979; **44:** 545–557.
2. Herdorf AJ, Edie R, Malm JR, Hoffman BF, Rosen MR. Electrophysiologic properties and responses to pharmacologic agents of fibers from diseased human atria. *Circulation* 1976; **54:** 775–779.
3. Allessie MA, Lammers WJEP, Bonke FI, Hollen J. Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation.

In: Zepes DP, Jalife J, editors. Cardiac electrophysiology and arrhythmia. New York: Grune and Stratton, 1985; 265–275.
4. Cox JL, Schuessler RB, D'Agostino HJ Jr, Stone CM, Chang BC, Cain ME, et al. The surgical treatment of atrial fibrillation. Ⅲ: Development of a definitive surgical procedure. *J Thorac Cardiovasc Surg* 1991; **101:** 569–583.
5. Cox JL, Jaquiss RDB, Schuessler RB, Boineau JP. Modification of the maze procedure for atrial flutter and atrial fibrillation. Ⅱ: Surgical technique of the maze Ⅲ procedure. *J Thorac Cardiovasc Surg* 1995; **110:** 485–495.
6. Kosakai Y, Kawaguchi AT, Isobe F, Sasako Y, Nakano K, Eishi K, et al. Cox maze procedure for chronic atrial fibrillation associated with mitral valve disease. *J Thorac Cardiovasc Surg* 1994; **108:** 1049–1055.
7. Mokadam NA, McCarthy PM, Gillinov AM, Ryan WH, Moon MR, Gaynor SL, et al. A prospective multicenter trial of bipolar radiofrequency ablation for atrial fibrillation: Early results. *Ann Thorac Surg* 2004; **78:** 1665–1670.
8. Sueda T, Nagata H, Shikata H, Orihashi K, Morita S, Okada K, et al. Simple left atrial procedure for chronic atrial fibrillation associated with mitral valve disease. *Ann Thorac Surg* 1996; **62:** 1796–1800.
9. Sueda T, Nagata H, Orihashi K, Morita S, Okada K, Sueshiro M, et al. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve disease. *Ann Thorac Surg* 1997; **63:** 1070–1075.
10. Imai K, Sueda T, Orihashi K, Watari M, Matsuura Y. Clinical analysis of results of a simple left atrial procedure for chronic atrial fibrillation. *Ann Thorac Surg* 2001; **71:** 577–581.
11. Sueda T, Imai K, Orihashi K, Takasaki T, Takahashi S, Kurosaki T. Late occurrence of atrial arrhythmia after the simple left atrial procedure for chronic atrial fibrillation in mitral valve surgery. *Ann Thorac Surg* 2010; **90:** 1959–1966.
12. Haissaguerre M, Jais S, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998; **339:** 659–666.
13. Sueda T, Imai K, Ishii O, Orihashi K, Watari M, Okada K. Efficacy of pulmonary vein isolation for the elimination of chronic atrial fibrillation in cardiac valvular surgery. *Ann Thorac Surg* 2001; **71:** 1189–1193.
14. Fugelman NY, Hasin Y, Katznelson N, Kriwiwsky M, Shefer A, Gotsman MS. Restoration and maintenance of sinus rhythm after mitral valve surgery for mitral stenosis. *Am J Cardiol* 1984; **54:** 17–27.
15. Atarashi H, Inoue H, Okumura K, Yamashita T, Kumagai N, Origasa H. Present status of anticoagulation treatment in Japanese patients with atrial fibrillation. *Circ J* 2011; **75:** 1328–1333.
16. Shiga T, Suzuki A, Naganuma M, Hosaka F, Shoda M, Hagiwara N. Clinical outcome in patients with paroxysmal or persistent atrial fibrillation receiving bepridil. *Circ J* 2011; **75:** 1334–1342.
17. Harada A, Sasaki K, Fukushima T, Tanaka T, Ikeshita T. Atrial activation during chronic atrial fibrillation in patients with isolated mitral valve disease. *Ann Thorac Surg* 1996; **64:** 104–112.
18. Morillo CA, Klein GJ, Jones DL, Guiraudon CM. Chronic rapid atrial pacing: Structural, functional, and electrophysiological characteristics of a new model of sustained atrial fibrillation. *Circulation* 1995; **91:** 1588–1595.
19. Kalifa J, Tanaka K, Zaitsev AV, Warren M, Vaidyanathan R, Auerbach D, et al. Mechanisms of wave fractionation at boundaries of high-frequency excitation in the posterior left atrium of the isolated sheep heart during atrial fibrillation. *Circulation* 2006; **113:** 626–633.
20. Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavaku T, et al. A new approach for catheter ablation of atrial fibrillation: Mapping of the electrophysiologic substrate. *J Am Coll Cardiol* 2004; **43:** 2044–2053.
21. Jais P, Haissaguerre M, Shah DC, Chouairi S, Clementy J. Regional disparities of endocardial atrial activation in paroxysmal atrial fibrillation. *Pacing Clin Electrophyisiol* 1996; **19:** 1998–2003.
22. Papone C, Manquso F, Vicedamini G, Guqilotta F, Santinelli O, Ferro A, et al. Prevention of iatrogenic atrial tachycardias after ablation of atrial fibrillation: A prospective randomized study comparing circumferential pulmonary vein ablation with a modified approach. *Circulation* 2004; **110:** 3036–3042.