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Electrophysiological Analysis of Chronic Atrial Fibrillation Associated with Mitral Valve Disease by Using Spectral Analysis

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ABSTRACT

Several authors have suggested that periodic activation is related to maintenance of atrial fibrillation (AF). The aim of this study was to examine periodic electrical activations in both atria that may lead to the generation and maintenance of AF associated with valvular diseases by means of fast Fourier transform (FFT) analysis. Atrial electrograms (AEGs) were analyzed in 15 persistent AF patients, who underwent pulmonary vein orifice (PVO) isolation with mitral valve surgery. Intraoperatively, AEGs of 4 seconds duration were acquired at 48 epicardial sites, 24 each from the right and left atrium (RA, LA). Dominant peaks (DPs) examined using FFT were present in 26% of all sampling points (380/1440). Prominent clustering of DPs was mostly observed on the LA. The mean AF cycle length (mAFCL) estimated from DP frequency was significantly shorter in LA than that in RA (178 ± 32 msec vs 247 ± 58, p = 0.0003). The shortest AF cycle length in each patient was mainly found in the LA. The PVO isolation procedures successfully eliminated AF in 87% of patients (13/15). In cases of recurred AF (2/15), the difference in mAFCL between bilateral atria was significantly smaller than in the case of successful AF elimination (17 ± 7 msec vs 76 ± 56, p = 0.042). FFT analysis of intraoperative mapping data clarified that periodic activity was present predominantly in LA. It may be possible to predict the efficacy of surgical procedures for eliminating AF using this technique.

Key words: *Chronic atrial fibrillation, Electrophysiology, Fast Fourier transform analysis, Surgical ablation*

Atrial fibrillation (AF) is most common among sustained cardiac arrhythmias in elderly patients, and is prevalent especially in patients with mitral valve diseases[15,24]. During the past decade, non-pharmacological therapies have emerged as AF treatments. Surgical procedures such as the Maze procedure[7] and its modifications[5,19] have proved to eliminate AF successfully in the majority of patients. Catheter ablation with radiofrequency energy has also been shown to terminate AF in selected groups of patients[12,13]. In patients with mitral valve diseases, AF has been eliminated by surgical procedures solely on the left atrium[4,11,30] that aimed to isolate the triggering activities of AF situated in the left atrium, and reduce the various factors which sustain AF. However, little is known about the electrophysiological mechanisms of human chronic AF on which these interventional strategies should be based.

Although atrial activation patterns characterized by irregular and fragmented electrical activity have been described as "disorganized" or "random"[1,6,18,21], recent investigations have demonstrated that AF is not completely random[3,14,28]. However, it is not easy to analyze atrial activation and its propagation patterns during AF, since even "chaotic patterns" are not well defined. Therefore, frequency analysis was applied to investigate periodic atrium activities instead of determining the activation time. Periodic activity concealed in apparently chaotic patterns is expressed as peak a formation in spectral analysis. In fact, spatial organization on the human right atrium has been demonstrated by spectral analysis of signals recorded by bipolar electrograms during AF. An experimental study with an acute animal model of AF showed spatiotemporal organization on both atria using spectral analysis

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of recorded signals[3,28].

Analyses of AF in the frequency domain have demonstrated multiple narrow-band peaks, often with a single dominant peak suggesting that a substantial portion of the atria are activating at this frequency, which are spatially ordered[28]. However, there are few studies regarding the anatomical distribution of dominant peaks in human chronic AF. This study aimed; 1) to examine the periodicity of atrial activities and its topical distribution in human persistent AF using spectral analysis and 2) to correlate the above results with the clinical outcomes of surgical intervention in cases of chronic AF associated with mitral valve diseases.

MATERIALS AND METHODS

Patient Characteristics

Fifteen consecutive patients who had chronic AF associated with mitral valve diseases indicated for surgery were enrolled in the study. Transesophageal echocardiography was used for intraoperative monitoring. Patients with diagnosed intracardiac thrombi during this period were excluded from the study. Table 1 shows the profiles of the patients. There were 3 men (20%) and 12 women with an average age of 62.3 years (range, 24 to 82 years). All patients had chronic AF refractory to medical treatment for 4 months to 20 years (average, 8.1 years). Nine of the patients had rheumatic mitral stenosis with or without mitral regurgitation, and 6 had mitral regurgitation secondary to degenerative valvular disease. Fourteen patients had other valvular diseases. Seven patients had tricuspid regurgitation (TR), 3 had aortic regurgitation (AR), 3 had TR with AR and 1 had TR with aortic stenosis. The clinical backgrounds of the patients are listed in the table. The cardio-thoracic ratio (CTR), duration of AF, left atrial dimension (LAD) and f-wave amplitude of lead V_1 (V1-f) were acquired as preoperative factors.

Mapping Protocol and Data Acquisition

After the induction and maintenance of anesthesia, the heart was exposed through a mid-line sternotomy. Before cardiopulmonary bypass was initiated, atrial epicardial mapping was performed with two commercially manufactured card-type electrodes (TE-125C, Epicardial Mapping Electrode, Fukuda-Denshi Co. Inc., Tokyo, Japan). Each had 24 bipolar electrodes, each of which consisted of a pair of electrodes (0.6 mm in diameter and embedded at a distance of 1.5-mm). The bipolar electrodes were mounted in a 4 by 6 matrix on a flexible rectangular plastic sheet (33 × 45 mm) with intervals every 7 mm in both directions. Each of the two card-type electrodes were placed on the free wall of the right atrium (RA) including crista terminalis and on the left atrium (LA) including the ligament of Marshall (Fig. 1). Atrial AF electrograms were recorded simultaneously using a cardiac mapping system (modified HPM-7100, Fukuda-Denshi Co. Inc., Tokyo, Japan). With conventional electrocardiographic filtering (0.16–500 Hz) and a digital sampling rate of 1000Hz, the data were recorded for 4096 milliseconds (msec) at 48 epicardial points and stored after appropriate amplification as a data file in a hard disk at 16-bit resolution. Data were collected twice in each patient for later analysis. The data consisted of 1440 recordings (15 patients × 2 times/patients × 48 points), 4096 msec each in recording length.

Analysis of Mapping Data

A total of 30 data files were analyzed by using

Table 1. Patient profiles

Case #	Sex	Age	Mitral valve diseases	V1-f (mV)	CTR (%)	LAD (mm)	dur. of AF (month)
1	f	61	R (III)+S	0.12	58	52	60
2	m	62	R (IV)	0.10	50	45	240
3	m	24	R (III)	0.30	58	60	48
4	f	62	R (III)+S	0.16	59	62	15
5	f	82	R (III)+S	0.08	69	65	144
6	m	50	R (II)+S	0.05	68	61	156
7	f	75	R (III)	0.25	70	48	24
8	f	73	R (I)+S	0.05	77	97	216
9	f	56	R (II)	0.10	58	48	240
10	f	53	S	0.08	56	50	92
11	f	61	S	0.15	55	49	24
12	f	63	R (I)+S	0.08	40	37	36
13	f	64	R (IV)	0.02	63	57	120
14	f	75	R (I)+S	0.25	64	57	4
15	f	74	R (II)	0.08	47	50	48

Mitral valve diseases and preoperative clinical factors are shown. The numbers in parentheses indicate severity of regurgitation. CTR: cardio-thoracic ratio, dur. of AF: duration of atrial fibrillation, f: female, LAD: left atrial dimension measured with transthoracic echocardiography, m: male, R: regurgitation, S: stenosis, V1-f: f-wave amplitude of lead V_1 on surface electrocardiogram.

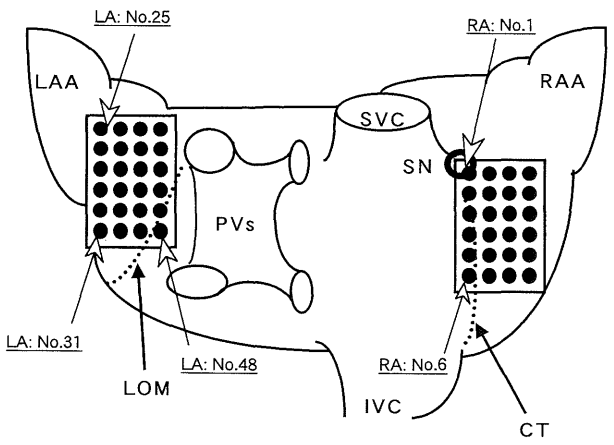

Fig. 1. Schematic illustration showing mapping points. Both atria are displayed from a back view. A pair of rectangular card-type electrodes was placed on the free wall of both atria. Each had 24 bipolar electrodes on a flexible plastic sheet. Bipolar electrodes were serially numbered as shown. CT: crista terminalis, IVC: inferior vena cava, LA: left atrium, LAA: left atrial appendage, LOM: ligament of Marshall, PVs: pulmonary veins, RA: right atrium, RAA: right atrial appendage, SN: sinus node, SVC: superior vena cava.

an off-line personal computer (CPU: PowerPC, Apple Computer Inc.). After the data were processed with a digital bandpass filter (0.5 to 60 Hz), spectral analysis was performed using a fast Fourier transform (FFT) with a commercially available software package (HyperWave 2.17, Kissei Comtec Co. Ltd., Tokyo, Japan). The size of the data set subjected to FFT was 4096 points, equal to the data points on one data file from an individual epicardial point. In order to minimize the artifacts at the onset and offset of signals, and to detect the lower peak formation, a Hunning window was applied. The signal was then subjected to a 4096-point FFT (with a spectral resolution of 0.24Hz) and displayed as a power spectrum by calculating the squared magnitude of each sample frequency.

Following FFT, the dominant peak frequencies were determined according to the definition described below. To minimize the effects caused by artificial ventilation, and other artifacts such as a harmonic frequency, only the content in the 1-to 10-Hz range (in the 60-to 600-beats/min) was analyzed. When the power of the maximum peak was larger than 20% of the total power within this range, the peak was defined as a "single dominant peak (SD-peak)". If the power of the second peak was larger than a half power of the maximum power peak, the peaks were defined as "multiple", not "single", dominant peaks. The cycle length of local atrial activation was calculated from all SD-peaks. The correlations between the cycle length and clinical preoperative factors were also analyzed.

Dominant Peak Detection

The periodicity of atrial activation was examined using spectral analysis at 48 points. Three examples are shown in Fig. 2. Bipolar electrograms (EGs) from each epicardial sampling point are shown on the left and the corresponding power spectrum (FFT) on the right. Because the amplitude of EGs varied among sampling points and cases, the EG was arbitrarily scaled along the ordinate to conveniently present three examples.

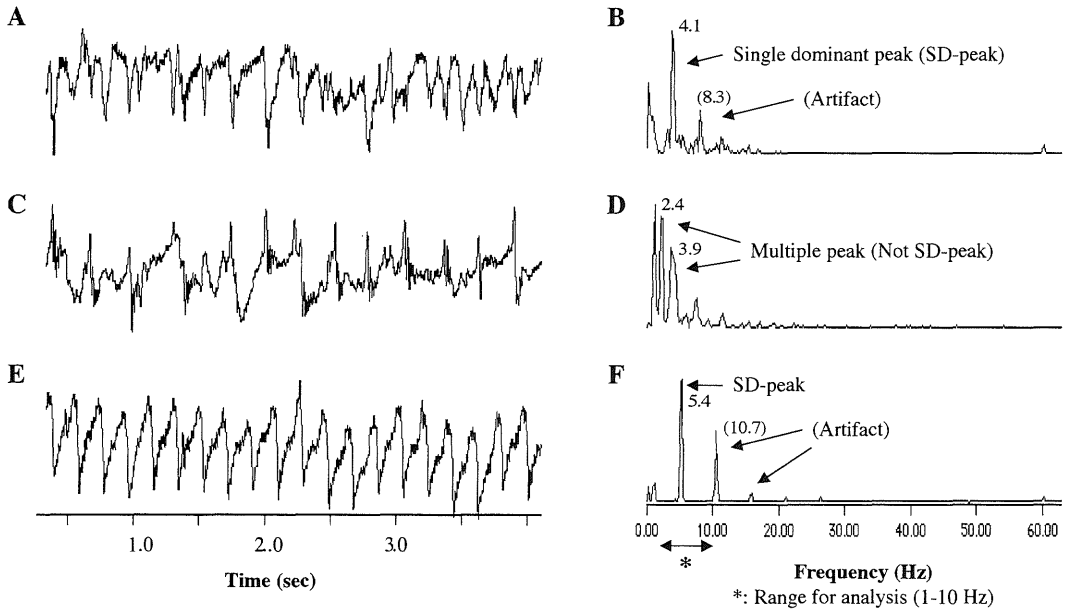

Fig. 2. Bipolar electrograms with corresponding spectral analysis data.
Bipolar electrograms are shown on the left. The corresponding frequency spectra produced by fast Fourier transform (FFT) are shown on the right. B and F are examples of single dominant peaks (SD-peak), while D shows a multiple peak.

Similarly in FFT, the power axes are not the same because the total power varied according to the amplitude of the bipolar EG. Although the bipolar EG of Fig. 2A apparently shows irregular electrical activity, the FFT (Fig. 2B) 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). Fig. 2D is another example of multiple peak formation. Although two narrow-band peaks are apparent, the frequency of the second peak (3.9 Hz) is not double of that of the maximum peak. The bipolar EG of Fig. 2E demonstrates regular and repetitive atrial activation, and the FFT (Fig. 2F) shows a sharp, discrete peak. The second to fifth harmonic peaks are clearly shown (artifacts).

Surgical Procedures and Clinical Analysis

Every patient underwent pulmonary vein orifice isolation (PVO isolation) to eliminate chronic AF using a standard cardiopulmonary bypass with mild hypothermia and cold blood cardioplegia. Following establishment of the cardiopulmonary bypass, a right-sided left atriotomy was extended toward the left margin of the left pulmonary veins without excision of the left atrial appendage. Cryoablation (–60°C, for 3 min) was applied with a specially designed T-shaped cryoprobe (Shiraimatsu Co. Ltd., Osaka, Japan; 20 mm long and 8 mm wide) to complete the isolation line around the PVO (Fig. 3). Subsequently, mitral valve replacement with mechanical prosthesis was performed in all patients. In 13 patients, concomitant surgical intervention was performed, including tricuspid annuloplasty (TAP) in 7 cases, aortic valve replacement (AVR) in 3 cases and TAP and AVR in 3 cases. All patients in this study were operated on by the same surgical team.

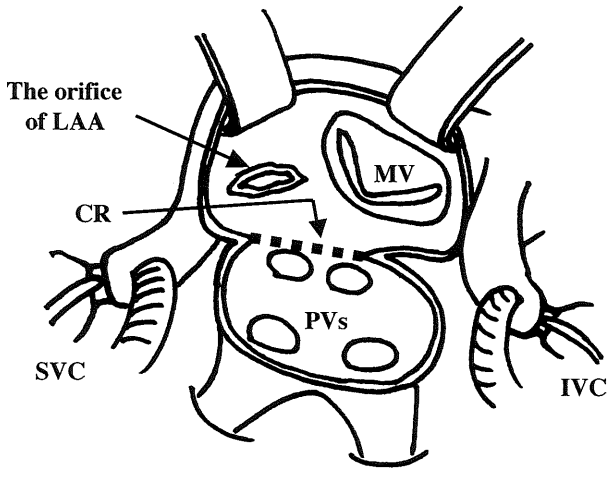

Fig.3. Schema of the pulmonary vein orifices isolation procedure.
The four pulmonary veins and a part of left atrium were electrically isolated via surgical incision and cryoablation (dotted line) without excision of the left atrial appendage. CR: cryoablation; IVC: inferior vena cava; LAA: left atrial appendage; MV: mitral valve; PVs: pulmonary veins; SVC: superior vena cava.

The postoperative results were evaluated by postoperative cardiac rhythm: sinus rhythm or atrial fibrillation. The preoperative clinical factors (CTR, duration of AF, LAD and V1-f on an surface electrocardiogram) and intraoperative electrophysiological data were analyzed in the light of the postoperative results.

Informed Consent and Statistical Analysis

Informed consent for the intraoperative mapping and surgical procedure was obtained from each patient. The results are expressed as means ± standard deviation. Continuous variables were compared using the nonparametric Mann-Whitney's U test. Proportions were compared with the chi-square test. A p value < 0.05 was considered significant. The statistical analysis was performed with a software package (StatView J-4.5; Abacus Concepts, Inc., Berkeley, Calif.).

RESULTS

Presence of Periodic Activity on the Atrium

Using spectral analysis of EGs, dominant peaks were present in 26.4% of all sampling points (380/1440 points, Table 2) with a mean peak frequency of 5.39 ± 1.40 Hz, ranging from 2.20 to 9.28 Hz (132 to 557 beats/min). All patients had dominant peaks at more than two points on the left atrium and one patient (case #1) had no peak on the right atrium. Comparing both atria, SD-peaks were detected more frequently on the left atrium (21.4% vs 31.4%, $p<0.0001$). Fig. 4 shows the distribution of dominant peaks on both atria. Prominent clustering of dominant peaks was observed mainly on the left atrium, especially around the base of the appendage. These findings suggest that periodic activity occurs predominantly on the left atrium.

Cycle Length of Periodic Activity and its Correlation with Clinical Parameters

The cycle length of local atrial activation was determined at individual sampling points based on every detectable single peak. The mean atrial fibrillatory cycle length (mAFCL) on each of two

Table 2. Presence of dominant peaks (N = 15)

Site	Dominant peak
Total (48 points)	380/1440 (26.4%)
RA (24 points)	154/ 720 (21.4%) †[1]
LA (24 points)	226/ 720 (31.4%) †[2]

Single dominant peaks were detected at more than 25% of the analyzed points. There were more dominant peaks ($p<0.0001$, †[1] vs †[2]) at the left atrium.

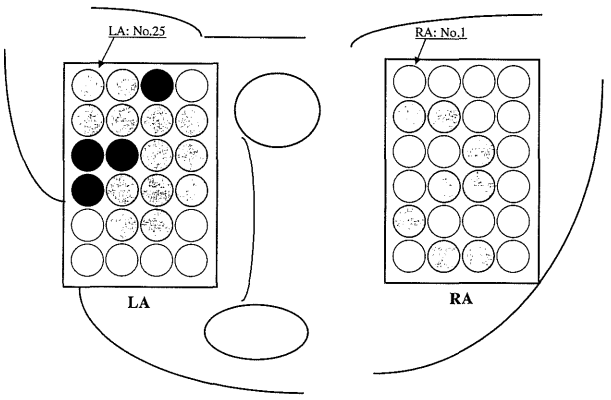

Fig. 4. Distribution of dominant peaks at both atria. The closed (black) and dark (gray) circles shown on each atrial epicardial point indicate high incidence of dominant peak appearance (closed: >50% / 24 data files, dark: 25–50% / 24 data files). Note the prominent clustering of dominant peaks on the LA free wall region, in contrast to the scarce clustering on the RA. LA: left atrium, RA: right atrium.

atria was calculated in each patient. The mAFCL of each atrium and the shortest AF cycle length for each patient are shown in Table 3. The mAFCL ranged from 173 to 374 msec at the RA, and from 131 to 268 msec at the LA. The mAFCL of the LA was always shorter than that of RA for each patient. The averaged mAFCL from the LA of all patients studied (the lowest row in Table 3) was significantly shorter than that from the RA (178 ± 32 vs 247 ± 58, p = 0.0003). The shortest cycle length ranged from 124 to 256 msec (3.9 to 8.1 Hz). The point where the shortest cycle length was recorded were mostly situated on the LA, and these points coincided with those at dominant peaks, except in cases #6 and #14.

The electrophysiological parameters (i.e. the mAFCL of each atrium, the shortest CL and the difference in mAFCL between both atria) were correlated with the preoperative clinical factors (i.e. CTR, duration of AF, LAD and amplitude of V1-f). Fig. 5 shows the correlation between the mAFCL of the LA and f-wave amplitude in lead V_1 of a preoperative surface electrocardiogram (R^2 = 0.300, p = 0.033). There was no significant correlation between mAFCL and other parameters.

Clinical Outcomes after the Surgical Procedure

There was no mortality or morbidity following PVO isolation. The overall rate of AF disappearance induced by this surgical procedure was 87% (13/15), with the follow-up period ranging from 1 to 15 months. Although AF remained in two patients (case #8 and #13) postoperatively, the remaining 13 patients maintained sinus rhythm. To elucidate any factors relating to the operative outcome, we divided the subjects into a sinus rhythm (SR) group and a recurred atrial fibrillation (AF) group and compared the electrophysiological parameters quantitatively between these two groups. In the AF group, the difference in mAFCL between the atria was significantly smaller than that of SR group (17 ± 7.0 msec vs 76 ± 56 msec, p = 0.042). The scattered display of the relationship between RAmAFCL and LAmAFCL is shown on Fig. 6.

Table 3. Cycle length in each patient

Case #	RAmAFCL (msec)	LAmAFCL (msec)	ΔmAFCL (msec)	Shortest CL (site) (msec)
1	275	197	78	124 (LA)
2	316	186	130	157 (LA)
3	247	214	33	186 (LA)
4	225	164	61	152 (LA)
5	244	162	82	152 (LA)
6	181	151	30	108 (RA)
7	319	268	51	256 (LA)
8	173	161	12	146 (LA)
9	247	160	87	157 (LA)
10	217	186	31	186 (LA)
11	283	131	152	124 (LA)
12	191	155	36	152 (LA)
13	209	187	22	178 (LA)
14	199	180	19	164 (RA)
15	374	169	205	124 (LA)
Average: RA = 247 ± 58 msec LA = 178 ± 32 msec (p = 0.0003)				

The cycle length was calculated from all detected single peaks and mean atrial fibrillatory cycle length (mAFCL) was calculated on each atrium of each patient. The mAFCL of the left atrium (LA) was shorter than that of the right atrium (RA) in all patients. The site with the shortest cycle length (CL) was placed on the LA, except in cases #6 and #14. [ΔmAFCL] = [(LAmAFCL)-(RAmAFCL)].

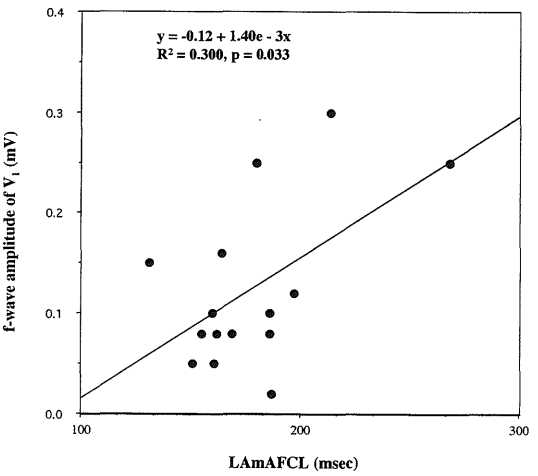

Fig. 5. Correlation of the mean atrial fibrillatory cycle length of the left atrium and f-wave amplitude of lead V_1 on preoperative surface electrocardiograms.
From the quantitative assessment between mean cycle length converted from spectral analysis and the clinical background of the patients, there was a significant correlation between the mean AF cycle length of the LA and f-wave amplitude of lead V_1.

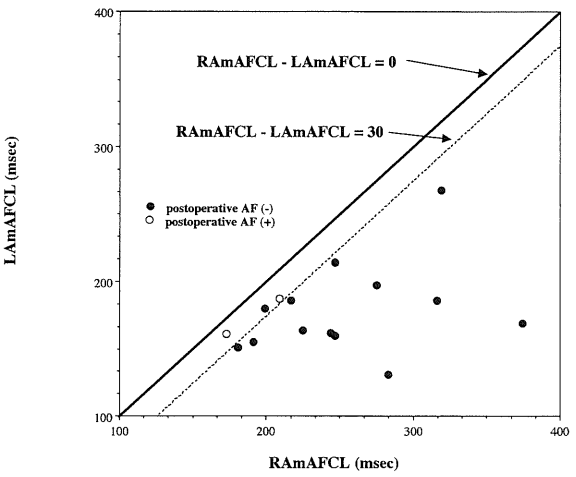

Fig. 6. A scattered display of right atrial and left atrial mean atrial fibrillatory cycle lengths with operative results.
The left atrial mean atrial fibrillatory cycle length (LAmAFCL) was shorter than right atrial mean atrial fibrillatory cycle length (RAmAFCL) in all patients (see Table 3). Two patients (case #8 and #13) demonstrated persistent AF postoperatively (shown as ○ on the figure) and the remaining 13 patients maintained sinus rhythm (●). There was no postoperative AF when [(RAmAFCL)-(LAmAFCL)] > 30 msec.

DISCUSSION

This is the first study to analyze the activities in both human atria with spectral analysis. This method has enabled us to recognize that highly regular activation is present in a portion of the atrial region, in spite of apparently irregular patterns on the conventional surface electrocardiogram. Using this analysis, such periodic activity was mainly found on the LA in AF patients associated with mitral valve disease. This finding is compatible with the clinical outcome that AF turned to sinus rhythm only with PVO isolation in the majority of patients.

Previous Electrophysiological Work on AF

The mechanisms underlying AF in humans are not yet fully understood. At the beginning of this century, it was believed that the irregular contractions of the atria were caused by either single or multiple ectopic foci[8,26]. This concept was challenged in the 1920's by Lewis[20] and Garrey[9], and they concluded that reentry was the true mechanism of AF. The debate on ectopic foci versus reentry continued for some decades. In 1962, the multiple-wavelet hypothesis of AF was described by Moe et al[21]. They hypothesized, on the basis of computer simulations, that fully developed fibrillation would be a state in which many randomly wandering wavelets coexisted. After Moe's proposal, experimental evidence for this multiple wavelet hypothesis was provided by Allessie et al[1,18]. However, more recent studies that applied ridge statistical methods to long episodes of endocardial recordings have provided evidence that AF is not random[3,10]. From the experimental study reported by Schuessler et al[27], atrial rapid repetitive responses after a single extrastimuli in the presence of high concentrations of ACh were characterized by multiple reentrant circuits. However, such multiple wavelets failed to perpetuate, and over time, sustained fibrillation was the result of a relatively stable single reentrant circuit. Skanes et al[28] used high-resolution video imaging, ECG recordings, and spectral analysis in a Langendorff-perfused sheep heart to identify sequential wave fronts with temporal periodicity and similar spatial patterns of propagation. They clearly demonstrated that wavelets with similar spatial patterns of propagation can activate regions of the atrium with a regular temporal cycle during AF. Taken together, these studies provided strong evidence that AF is not an entirely random phenomenon.

On the other hand, there were some problems in the analysis of atrial AF potentials. The activation patterns of AF have been described as disorganized or random because of their irregular and fragmented (not discrete) electrograms[1,6,18,21]. Wells et al[31] pointed out in their report, analyzing bipolar atrial electrograms following open heart surgery, that human AF is not an electrophysiologically homogeneous process. They also described the existence of totally chaotic activations (type III or IV in their classification). Therefore, they were not able to determine the activation time and atrial rate accurately in these cases. Recent studies have adopted an algorithm for automatic detection of intrinsic negative deflection of the electrograms[14,18]. This algorithm was originaly introduced to analyze ventricular activities during ventricular tachycardia, which exhibited more discrete and large potentials than atrial activities[23]. In the present study, therefore, we avoided detecting the activation time, but adopted spectral analysis to observe the atrium's whole electrical activities.

Spectral Analysis of Atrial Activity at Multiple Points in AF

In regard to the local atrial periodicity of AF associated with organic heart disease, there are few previous studies that used the technique of spectral analysis. Previous investigations analyzed the frequency content of the surface electrocardiogram fibrillatory baseline. Slocum and coworkers[29] observed power spectra with a distinct peak in the 5-to 9-Hz range (300 to 540 beats/min) using a signal processing technique to make electrocardiographic recordings of AF. Bollmann et al[2] showed in their report that the mean peak frequency of the fibrillatory activity was 348 ± 72 beats/min (range 228 to 540) in V1 using QRS subtraction and FFT. In the current study, the FFT display and findings were similar to previous

reports using spectral analysis[2,17,25,28]. The presence of a dominant narrow-band peak suggests that a substantial portion of the atria is activated at that frequency. We analyzed the content in the 1-to 10-Hz band because the cycle length of human atrial periodic action has been shown to be within this range in previous studies. Throughout the analysis of FFT display, we arbitrarily set the cut-off line at 20 % of total power in detecting the peak, in order to eliminate noise.

In two recent reports on surgical cases using a small number of multiple bipolar electrode recordings[14,30], regular and repetitive activation was shown in the LA in AF patients with isolated mitral valve diseases. In the current study, spectral analysis demonstrated prominent clustering of dominant peaks around the LA free wall, in spite of the small number of electrodes and rather limited area of the atrium covered. From the display of peak distribution (Fig. 4), a high incidence (> 25%) of dominant peaks was observed at most of epicardial points on the LA (18/24, 75%), while in only a portion of points on the RA (8/24, 33%). These findings indicate that periodic electrical activities exist mainly on the LA, rather than on the RA in cases of AF associated with mitral valve diseases. It should be stressed that the quantitative presentation of periodicity is helpful in understanding the electrophysiological characteristics of the fibrillating atrium.

Atrial Cyclelength and Fibrillation Frequency

Several experimental and clinical studies have suggested that a short atrial cyclelength is critically important for the initiation and perpetuation of AF[2,14,22,30]. Morillo and coworkers[22] reported, in their experimental study of canine rapid pacing model, that the shortest AFCL was uniformly seen in the area of the posterior LA and was consistently faster than the rest of the epicardial site. They also found a good correlation between the local epicardial effective refractory period and local AFCL (R^2 = 0.93). From these results, they concluded that the region with the shortest AFCL may be critical in the maintenance of AF. In our study, the shortest AFCL ranged from 124 to 256 msec, and was found mostly on the LA wall (Table 3). Although the point with the shortest AFCL was different among patients, it coincided with the region having dominant peaks. Comparing both atria, the mean AFCL was significantly shorter in the LA than in the RA (p = 0.0003). These findings are compatible with previous studies[14,30]. Spectral analysis may help locate the shortest AFCL, and can be useful in making a decision to conduct interventional strategies for the elimination of AF.

Relevance of Electrophysiological Analysis to Operative Outcomes

Electrical isolation of PVO via surgical measures resulted in an AF elimination rate of 87% (13/15), although the duration of follow-up was not long enough. In two cases of recurring AF, the mAFCL in the LA was very close to that in the RA, compared with the remaining 13 cases (Fig. 6). If the cut-off value of the mAFCL difference between LA and RA is assigned as 30 msec, as shown in Fig. 6, the electrophysiological findings can predict the surgical outcome (p = 0.0314: sensitivity 67%, specificity 100%), potentially enabling mapping-guided decision-making. These findings suggest that the differences in electrophysiological characteristics in the two atria may affect the operative result with PVO isolation.

In a previous human study[2], a strong positive correlation (r = 0.98) was shown between the right intra-atrial peak frequency and that of the QRS-subtracted electrocardiogram in lead V_1. However, there was little description of the relationship between potential in surface electrocardiograms and AFCL. The f-wave amplitude of lead V_1 was frequently evaluated as the preoperative predictor for the elimination of AF after surgery[16,19]. Isobe et al[16] reported, based on 30 of Maze procedure cases of chronic AF associated with mitral valve diseases, that low f-wave voltage at lead V_1 was a predisposing factor for AF persistence after surgery. A significant positive correlation was shown between the f-wave amplitude of lead V_1 and LAmAFCL in our study (Fig. 5). However, LAmAFCL was not a significant factor for recurrent AF. Although a non-invasive simple examination such as surface electrocardiography is important for evaluating preoperative conditions, it is not appropriate to rely on it totally, and detailed analysis is required to clarify the relationship between the indirect atrial potential and operative results.

Insight into the Mechanism Underlying Chronic AF

This study did not clarify the complete mechanism of chronic AF. However, our results showed that: 1) the periodicity of atrial activation predominantly resides in the left atrium, clearly demonstrated through the spectral analysis of multi-site simultaneous biatrial mapping; 2) solely electrical isolation of PVs, not the LA wall, resulted in recovery of sinus rhythm after several years of continued AF at a success rate similar to standard Maze procedures. If it is assumed that the PVs potentials drive the periodic actions of LA, the above-mentioned findings can be explained clearly. Importantly, two unsuccessful cases indicated the possibility of predicting recurring AF patients with spectral analysis of atrial activation in the operating theater in the near future. Since chronic AF is an arrhythmia with complicated mechanisms, further investigations with intraoperative atrial mapping, including the atrial septum, are

needed to elucidate new insight into its more detailed mechanisms.

Study Limitations

A card-type bipolar electrode has a fixed size and the mapping density is rather low. Since the atrial size varied among patients, the position of landmarks shown in Fig. 4 can be different among cases. To investigate the atrial potentials with further anatomical precision, an electrode system which can be flexibly tailored to fit the atrium of each individual patient is needed. The current mapping system is not suitable to investigate the potentials at the atrial septum. Whole atrium mapping, with a detailed periodicity of the atrium including the septum, was not feasible in this study.

Since chronic AF is an extremely complex and intricate arrhythmia, we should pursue further investigations with intraoperative atrial mapping. A more sophisticated mapping system, capable of high density data acquisition from a broader area of the atrium with a longer duration using fitted electrodes is required to analyze the detailed periodic activities of the atrium.

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