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Analysis of Heart Rate Variability before and after Catheter Ablation for Atrial Flutter with Complicating Atrial Fibrillation

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Efficacy of radiofrequency (RF) catheter ablation in suppressing atrial fibrillation (AF) was studied by analysis of heart rate variability (HRV) in 13 patients with atrial flutter complicated with AF. We treated these patients by RF ablation of the isthmus between the tricuspid valve annulus and the inferior vena cava to create a bidirectional conduction block. To analyze the HRV, 24-h ambulatory electrocardiographic monitoring was performed 1 day before, 1 day after and 1 month after the ablation. After the RF ablation of the isthmus, 7 patients continued to experience AF attacks, while the remaining 6 patients did not. We divided them into 2 groups, attacked by AF (AF group) and not attacked by AF (non-AF group), and analyzed HRV parameters. The results obtained were compared between the groups. One month after the ablation, the non-AF group showed a significantly higher average heart rate than the AF group. The HRV parameters indicating cardiac vagal nervous activities, such as the root-mean-square of differences, percentage of adjacent normal RR intervals and high frequency power, were significantly lower in the non-AF group 1 month after. Furthermore, the ratio of low frequency power to high frequency power, which is a measure for cardiac sympathetic nervous activity, was significantly higher in the non-AF group 1 month after. From these results, we postulate that the suppression of postoperative AF may involve vagal nerve suppression and sympathetic nerve activation.

Key words: atrial fibrillation; atrial flutter; catheter ablation; heart rate variability

Radiofrequency (RF) catheter ablation of the isthmus between the tricuspid valve annulus and the inferior vena cava (TVA-IVC isthmus) has become an effective procedure for radical treatment of common type atrial flutter (AFL). However, late recurrence of atrial fibrillation (AF) following successful ablation still remains an important clinical problem. Though RF ablation of AF has spread rapidly since Haissaguerre et al. (1998), pulmonary vein stenosis (Saad et al., 2003) and atrio-esophageal fistula (Pappone et al., 2004a) after ablation of AF were reported as severe complications. Also, pulmonary vein ablation of AF may predispose to proarrhythmias such as left atrial macroreentrant

Abbreviations: AF, atrial fibrillation; AFL, atrial flutter; AVNRT, atrioventricular nodal reentrant tachycardia; ECG, electrocardiography; HF, high frequency power; HRV, heart rate variability; LF, low frequency power; LF/HF, the ratio of LF/HF; pNN50, percentage of adjacent normal RR intervals; RF, radiofrequency; rMSSD, root-mean-square of differences; SDNN, SD of RR intervals; TVA-IVC isthmus, isthmus between the tricuspid valve annulus and the inferior vena cava

Table 1. Patient characteristics

Group	Patient	Age (year)	Sex	Cardiovascular diagnosis	Antiarrhythmic drug
AF group	Patient 1	66	Male	PAFL, PAF	Pilsicainide, Digitalis
	Patient 2	54	Male	PAFL, PAF	Cibenzoline
	Patient 3	78	Male	PAFL, PAF	None
	Patient 4	55	Female	PAFL, PAF, OMI	Bepridil, Flecainide
	Patient 5	57	Male	PAFL, PAF	Cibenzoline, Pilsicainide
	Patient 6	52	Male	PAFL, PAF	Cibenzoline
	Patient 7	48	Male	PAFL, PAF	None
Non-AF group	Patient 1	51	Male	PAFL, PAF	None
	Patient 2	45	Male	PAFL, PAF	Aprindine
	Patient 3	68	Male	PAFL, PAF, OMI	Pilsicainide, Digitalis
	Patient 4	65	Male	PAFL, PAF	Cibenzoline, Verapamil
	Patient 5	63	Female	PAFL, PAF	Aprindine, Digitalis
	Patient 6	74	Male	PAFL, PAF	Pilsicainide

OMI, old myocardial infarction; PAF, paroxysmal atrial fibrillation; PAFL, paroxysmal atrial flutter.

tachycardias (Pappone et al., 2004b). It has been reported that RF ablation for common type AFL of the TVA-IVC isthmus is effective in reducing the incidence of AF attacks (Feld et al., 1992; Lesh et al., 1994; Philippon et al., 1995; Saxon et al., 1996; Huang et al., 1998; Paydak et al., 1998; Tai et al., 1998; Nabar et al., 1999; Kumagai et al., 2000). Huang et al. (1998) reported that, in patients who experienced conversion of AF to AFL during antiarrhythmic drug treatment, ablation for AFL and continuation of pharmacologic therapy were effective means of maintaining sinus rhythm. As such, hybrid therapy is well-known and effective not only in patients experiencing a pharmacologic conversion of AF to AFL, but also in patients with both AF and AFL (Feld et al., 1992; Lesh et al., 1994; Philippon et al., 1995; Saxon et al., 1996; Paydak et al., 1998; Tai et al., 1998; Nabar et al., 1999; Kumagai et al., 2000). We wanted to characterize patients in which ablation for AFL is also effective in suppression of concomitant AF. In this regard, a number of reports have described the clinical features of such patients (Feld et al., 1992; Lesh et al., 1994; Philippon et al., 1995; Saxon et al., 1996; Paydak et al., 1998; Tai et al., 1998; Nabar et al., 1999; Kumagai et al., 2000). However, there is no report to characterize autonomic nervous function using heart rate variability (HRV) analysis in effective cases for suppression of concomitant AF after ablation for AFL. In the present study, changes in autonomic nervous function before and after ablation in the postoperative AF patients group were compared with the non-AF group using HRV analysis.

Subjects and Methods

Informed consent was obtained from all patients prior to 24-h ambulatory electrocardiography (ECG) 1 day before ablation.

Patient population

A total of 13 patients (11 males and 2 females, age 59.5 ± 9.7 years, duration of observation 6.5 ± 4 months) having had both AF and AFL before ablation, were selected by satisfying all the following criteria: i) subjective attacks of paroxysmal tachycardia (AF or AFL), ii) paroxysmal AF, iii) no use of autonomic drugs (β blockers, etc.), iv) no thyroid disease or valvular heart disease, v) the ablated site of the exact isthmus, excluding the posterior septum, and vi) no switchover of medication during the observation period. The observation period was from the day of ablation to September 11, 2004.

These patients were divided into 2 groups: 7 patients (6 males and 1 female, age 58.3 ± 9.2 years, duration of observation 5.9 ± 3.4 months) with paroxysmal AF recorded with 12-lead ECGs on paroxysmal attacks during the observation period after ablation (AF group) and 6 patients (5 males and 1 female, age 61.0 ± 9.9 years, duration of observation 7.2 ± 5.6 months) without AF (non-AF group) (Table 1). There was no significant difference in sex, age, observation period or clinical features between the 2 groups.

RF catheter ablation

After confirming the involvement of the TVA-IVC isthmus in the tachycardia circuit during AFL, a bidirectional conduction block line was created in the TVA-IVC isthmus by ablation. This ablation was performed in the portion of the isthmus between the 6 and 7 o'clock directions in the left anterior oblique view, using a 6-mm deflectable large tip catheter. Subsequently, cardiac pacing was performed from the low lateral right atrium and the coronary sinus, and the bidirectional block line in the TVA-IVC isthmus was confirmed using the 20-electrode halo catheter method (Poty et al., 1996) and the differential pacing method (Shah et al., 1999). One of the 7 patients in the AF group and 1 of the 6 patients in the non-AF group had been suffering from spontaneous AFL before ablation. For the other patients, ablation was performed after inducing AFL by programmed stimulation.

Analysis of HRV

One day just before, 1 day just after and then 1 month later after ablation, 24-h ambulatory ECG monitoring was performed using a 2-channel Holter monitor (Fukuda Denshi, Tokyo, Japan), and HRV was analyzed and evaluated using the ECG analytical software CHIRAM/MemCalc (GMS, Tokyo). The parameters determined were average heart rate (recorded by 24-h ambulatory ECG monitoring), time domain parameters and frequency domain parameters of HRV. The time domain parameters were SD of 5-min mean RR intervals (SDNN), root-mean-square of differences of adjacent RR intervals (rMSSD) and percentage of adjacent normal RR intervals > 50 ms different (pNN50). The frequency domain parameters were low frequency power (LF) ranging from 0.04 to 0.15 Hz, high frequency power (HF) ranging from 0.15 to 0.40 Hz and the ratio of LF to HF (LF/HF). Of these parameters, SDNN, rMSSD, pNN50 and HF were reported to indicate cardiac vagal nervous activities, and LF/HF to indicate cardiac sympathetic nervous activities (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

Statistical Analysis

Data were presented as the mean ± SD. Variables of average heart rate and HRV analysis were compared using unpaired *t*-test. A P value < 0.05 was considered statistically significant.

Results

RF catheter ablation

A bidirectional block was successfully created in all patients of both groups. Statistical difference was examined for the number of RF application times (AF group versus non-AF group; 6.2 ± 4.3 times versus 5.6 ± 4.0 times, not significant) and RF cumulative energy (AF group versus non-AF group; 21,962 ± 3,160 W•s versus 19,330 ± 2,966 W•s, not significant). There was no patient experiencing recurrent AFL during the observation period (Table 2).

Table 2. Results of RF catheter ablation

	AF group [*n* = 7]	Non-AF group [*n* = 6]
Bidirectional block	7/7	6/6
RF application*	6.2 ± 4.3	5.6 ± 4.0
RF cumulative energy†	21,962 ± 3,160	19,330 ± 2,966
AFL recurrence	0/7	0/6

Values are mean ± SD.
AF, atrial fibrillation; AFL, atrial flutter; RF, radiofrequency.
* (times)
† (W•s)

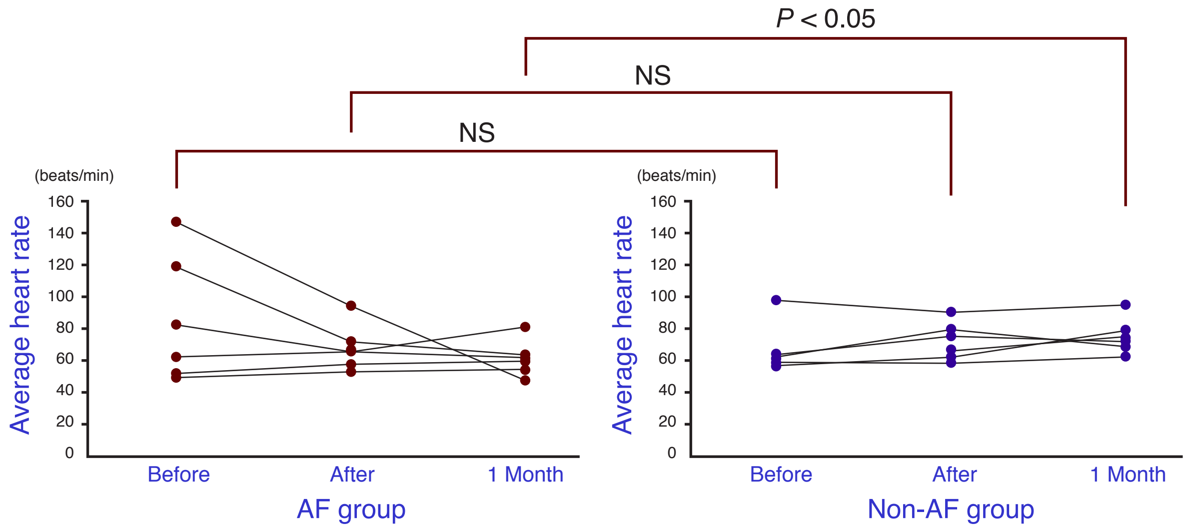

Fig. 1. The mean heart rate for the AF group and the non-AF group, just before, just after and 1 month after ablation. The non-AF group shows a significantly higher value 1 month after ablation. NS, not significant.

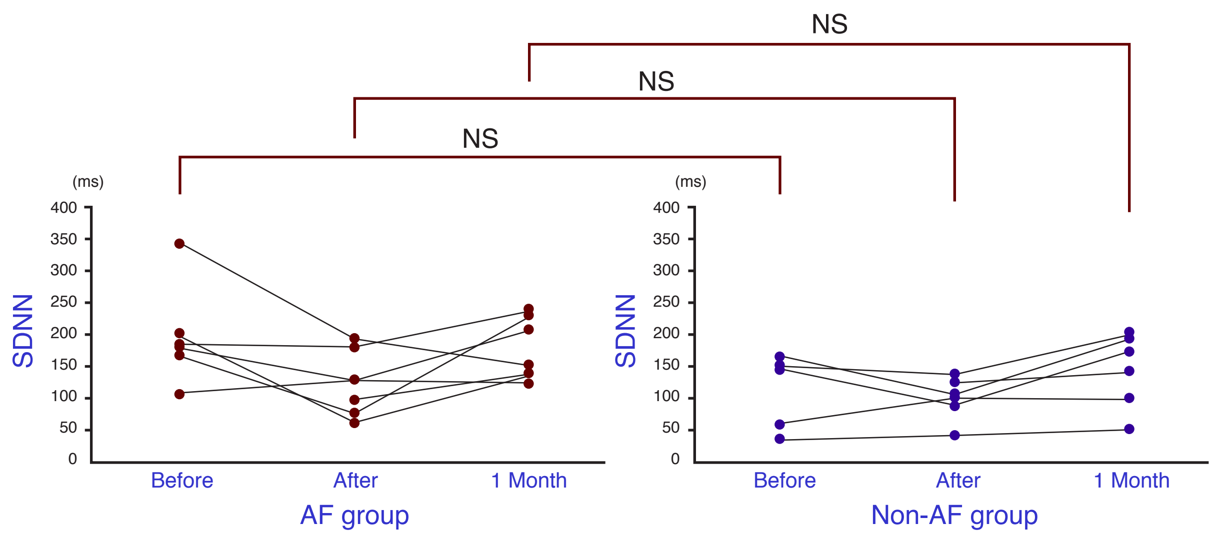

Fig. 2. The SD of RR intervals (SDNN) for the AF group and the non-AF group: 196.9 ± 78.3 versus 112.1 ± 59.0 ms just before ablation; 123.6 ± 48.8 versus 99.4 ± 32.6 ms just after ablation; and 174.9 ± 47.7 versus 143.6 ± 58.5 ms 1 month after ablation. Differences between groups are not significant (NS).

24-h Ambulatory ECG monitoring and average heart rate

Compared between the AF and the non-AF groups, the average heart rates just before ablation and just after ablation, 85.2 ± 39.4 versus 67.8 ± 16.7 beats/min and 67.3 ± 13.1 versus 71.8 ± 12.3 beats/min, respectively, showed no significant difference. The difference in average heart rate 1 month after ablation was significantly ($P < 0.05$) higher for the non-AF group, 61.3 ± 10.2 versus 74.8 ± 11.1 beats/min (Fig. 1).

Time domain parameters of HRV

The SDNNs just before, just after and 1 month after ablation compared between the AF and the non-AF groups were not significantly different, respectively (Fig. 2).

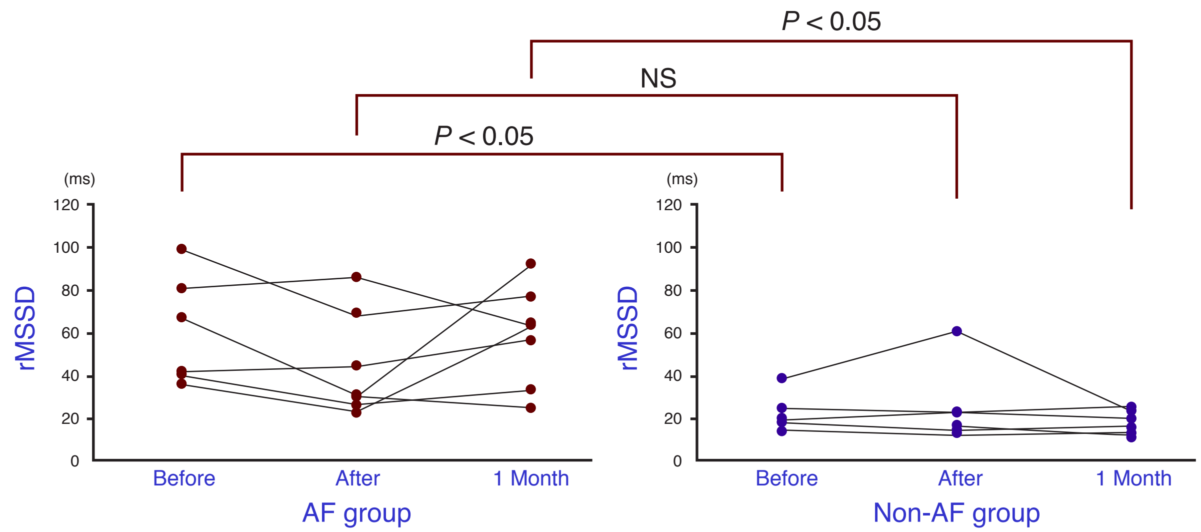

Fig. 3. The root-mean-square of differences (rMSSD) for the AF group and the non-AF group, just before, just after and 1 month after ablation. The non-AF group shows significantly lower values just before and 1 month after ablation. NS, not significant.

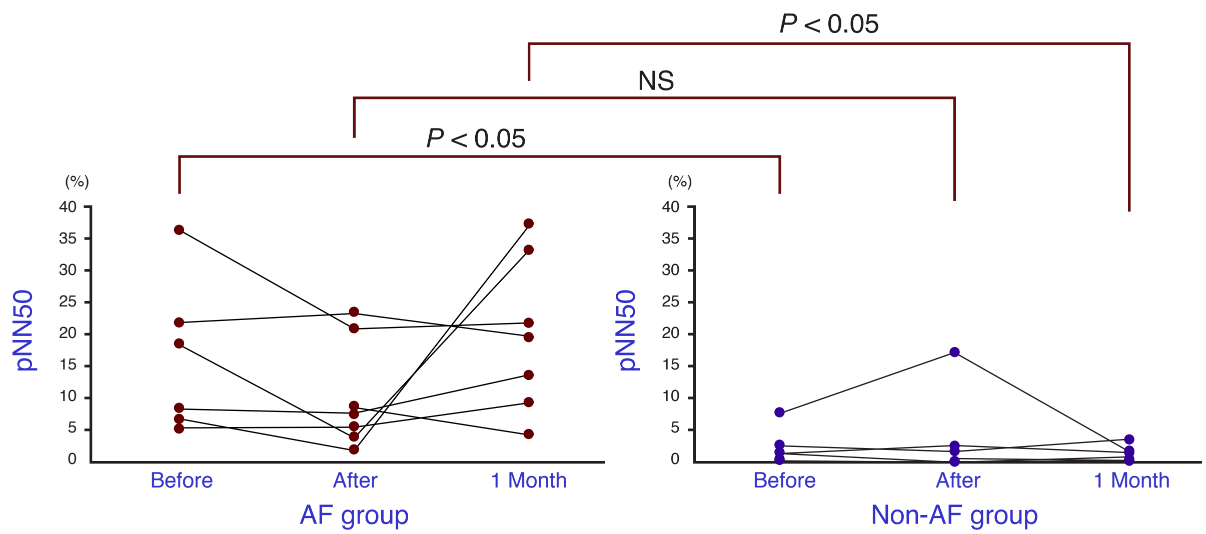

Fig. 4. The percentage of adjacent normal RR intervals (pNN50) for the AF group and the non-AF group, just before, just after and 1 month after ablation. The non-AF group shows significantly lower values just before and 1 month after ablation. NS, not significant.

The rMSSDs compared between the 2 groups just before ablation, 60.9 ± 25.6 versus 23.2 ± 9.6 ms, were significantly ($P < 0.05$) lower for the non-AF group, as well as levels 1 month after ablation, 59.1 ± 23.7 versus 18.0 ± 5.7 ms ($P < 0.05$). The difference in levels just after ablation, 44.4 ± 23.7 versus 24.7 ± 18.2 ms, was not significant (Fig. 3).

The pNN50s just before ablation and 1 month after ablation were 16.5 ± 11.9 versus 2.7 ± 3.0% and 20.0 ± 12.1 versus 1.4 ± 1.3%, respectively, showing significantly ($P < 0.05$ both) lower levels for the non-AF group. The levels just after ablation, 10.3 ± 8.4 versus 3.8 ± 6.7%, were not significantly different (Fig. 4).

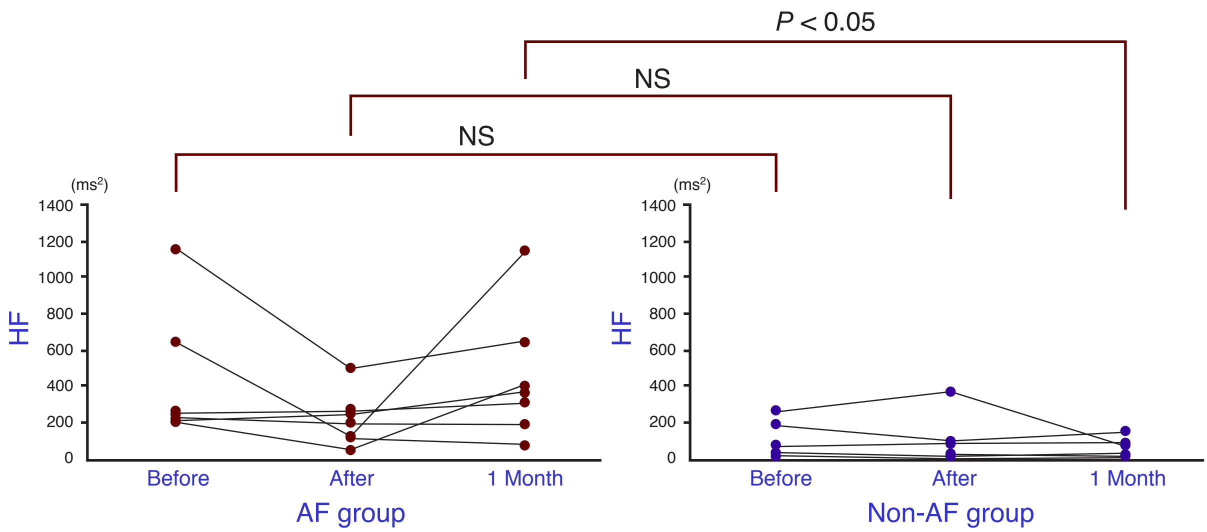

Fig. 5. The high frequency power (HF) for the AF group and the non-AF group, just before, just after and 1 month after ablation. The non-AF group shows a significantly lower value 1 month after ablation. NS, not significant.

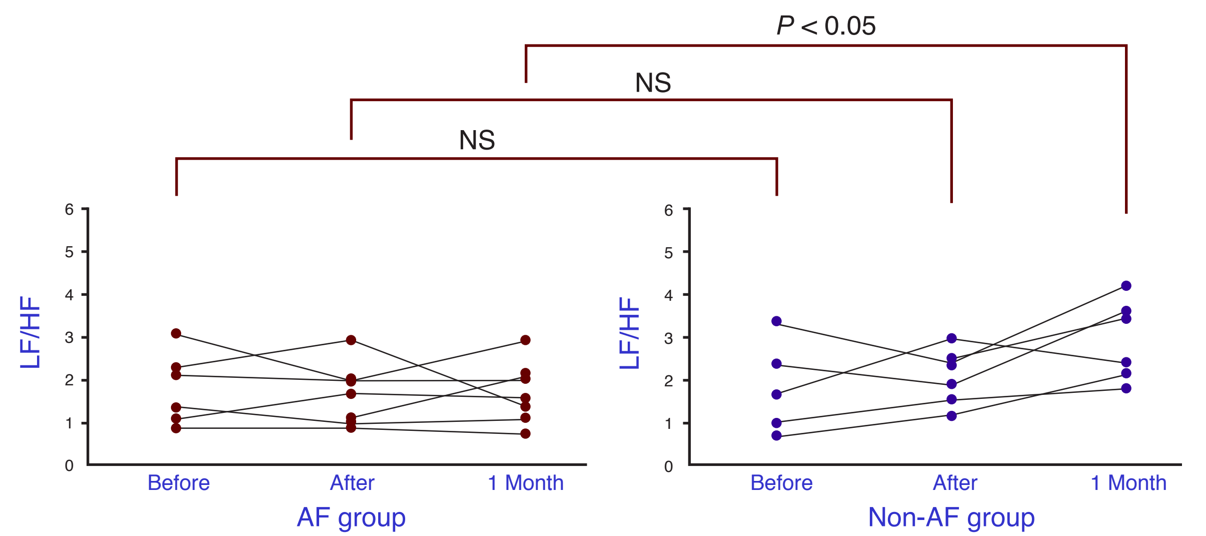

Fig. 6. The ratio of low frequency power/high frequency power (LF/HF) for the AF group and the non-AF group, just before, just after and 1 month after ablation. The non-AF group shows a significantly higher value 1 month after ablation. NS, not significant.

Frequency domain parameters of HRV

The HF levels compared between the groups were 462.3 ± 386.8 versus 115.8 ± 109.7 ms^2 just before ablation, 221.1 ± 150.7 versus 108.4 ± 137 ms^2 just after ablation and 460.4 ± 358.7 versus 62.2 ± 55.6 ms^2 1 month after ablation. The difference 1 month after ablation was significantly lower for the non-AF group (Fig. 5).

The compared LF/HF levels were 1.8 ± 0.8 versus 1.8 ± 1.1 just before ablation and 1.6 ± 0.7 versus 2.1 ± 0.7 just after ablation, showing no significant differences between the groups. The levels 1 month after ablation, 1.7 ± 0.7 versus 2.9 ± 0.9, were significantly ($P < 0.05$) higher for the non-AF group (Fig. 6).

Discussion

It has been reported that ablation for common type AFL, which circles between the tricuspid valve annulus and the inferior vena cava, is effective in reducing the incidence of AF attacks, and the percent incidence of AF after ablation of the TVA-IVC isthmus is reportedly variable, from 8% to 86% (Feld et al., 1992; Lesh et al., 1994; Philippon et al., 1995; Saxon et al., 1996; Paydak et al., 1998; Tai et al., 1998; Nabar et al., 1999; Kumagai et al., 2000). Regarding the identity of cases in which ablation of the TVA-IVC isthmus is effective in suppressing AF, Philippon et al. (1995) reported that the risk of postoperative AF was especially high for patients in whom sustained AF remained inducible after ablation of AFL, while Paydak et al. (1998) reported the same finding in the presence of both a past history of AF and a left ventricular ejection fraction of 50% or less. Nabor et al. (1999) reported low AF suppressing effects in patients frequently experiencing AF episodes before ablation. They also reported that there were 3 mechanisms for the coexistence of AF and AFL: i) a difference between the 2 atria, the right atrium showing AFL and the left atrium showing AF; ii) AFL in the right atrium becoming unstable or irregular and hence leading to AF; and iii) a time lag between AFL and AF. They concluded that in cases i) and ii) ablation for AFL was also effective against AF (Nabar et al., 1999).

Regarding the distribution of vagal nervous fibers to the cardiac sinoatrial node and atrioventricular node, relatively extensive investigations have been conducted. Randall and Ardell (1990) pointed out the importance of the atrial septum as the anatomical route for this distribution as the course of vagal nervous postganglionic fibers from the right pulmonary venous adipose tissue to the sinoatrial node passing between the 2 atria. Since the early days of the spread of ablation as a therapeutic technique, it has been known that some patients experience sinus tachycardia mainly after ablation of the fast pathway in atrioventricular nodal reentrant tachycardia (AVNRT), and possible disturbance of autonomic nervous function due to ablation has been postulated (Ehlert et al., 1992). Kocovic et al. (1993) investigated autonomic nervous function from the viewpoint of HRV after ablation for supraventricular tachycardia, and reported that the HF of HRV decreased only in AVNRT and septal ablation of the posterior septum accessory pathway. With regard to ablation for AFL, Li et al. (2002) reported that ordinary ablation of the TVA-IVC isthmus did not affect autonomic nervous function in terms of HRV. Kawamura et al. (2002) investigated differences related to AFL ablation sites, and reported that the HF of HRV decreased only in the site of the posterior septum, rather than in the ordinary TVA-IVC isthmus.

In the present study, we investigated HRV just before ablation, just after ablation and 1 month after ablation in order to characterize cases in which ablation for AFL was also effective in suppressing AF. As a result, significantly lower values of rMSSD and pNN50 were obtained from the non-AF group just before ablation. However, 1 month after ablation, a higher value of average heart rate, lower values of rMSSD and pNN50, a lower value of HF and a higher value of LF/HF were obtained for the non-AF group than for the AF group. These results demonstrate suppression of vagal nervous function and accentuation of sympathetic nervous function in the non-AF group 1 month after ablation. These effects were not attributable to ablation because the cases in which RF application was delivered to the atrial septum were excluded from the analysis to avoid the possible influence of ablation on the autonomic nervous system. As for why a significant difference became clear 1 month after ablation, we postulated i) changes in autonomic nervous function due to the disappearance of AFL and ii) a latent abnormality of autonomic nervous function becoming symptomatic. Although the mechanism remains unclear, these results suggested that analysis of HRV 1 month after ablation might enable selection of cases in which ablation of the TVA-IVC isthmus is also effective in the suppression the recurrence of AF. For appropriate follow-up, the case to require anticoagulant and antiarrthythmic drugs should be clarified. And we suppose that for patients with postoperative recurrent AF, drugs that suppress vagal nervous function and accentuate sympathetic nervous function might be more effective than other drugs.

In the present study, HRV was analyzed to evaluate autonomic nervous function in AFL patients with paroxysmal AF, whereas other means of evaluation for cardiac autonomic nervous function such as baroreceptor reflex and ^{123}I-metaiodobenzylguanidine scintigraphy were not used. Because of the many requirements for studying a population, the sample size of this study was not enough to ensure data reliability. Additionally, the study was conducted in a relatively short period, from just before and just after ablation to 1 month after ablation. Further investigation ranging over an extended period will be necessary.

Conclusion

To characterize the autonomic nervous function profiles in cases in which ablation for AFL is effective in suppressing concomitant AF, HRV was analyzed in patients with both AF and AFL. In the group with suppressed AF after ablation, a significantly higher value of average heart rate, significantly lower values of rMSSD, pNN50 and HF, and a significantly higher value of LF/HF were obtained 1 month after ablation, showing characteristic changes in autonomic nervous function.

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