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**Original Article**

# Atrial Fibrillation and Fragmented Atrial Activity in Sick Sinus Syndrome

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**Abstract:** We evaluated the relationship between paroxysmal atrial fibrillation and fragmented atrial activity in eighteen patients with sick sinus syndrome. Twelve patients had paroxysmal atrial fibrillation (group A), and six patients had no such dysrhythmia (group B). Fragmented atrial activity was recorded in 10 of the 12 patients (83%) in group A, but only 1 of the 6 patients (17%) in group B. The sensitivity, the specificity and the predictive value of the fragmented atrial activity to predict the paroxysmal atrial fibrillation were 83%, 71% and 83% respectively. In conclusion, fragmented atrial activity may be a good index to predict spontaneous paroxysmal atrial fibrillation in sick sinus syndrome.

**Key words:** Fragmented atrial activity, Atrial fibrillation, Sick sinus syndrome

There are three types of sick sinus syndrome. Type 1 is characterized by sinus bradycardia while Type 2 is characterized by sinus arrest or sinoatrial block. Type 3 is called bradycardiatachycardia syndrome and the most frequent tachyarrhythmia in this case is atrial fibrillation[1].

A marked fragmentation in atrial activity is often recorded by an intraatrial electrogram in not only patients with sick sinus syndrome, but also patients with paroxysmal atrial fibrillation[2]. Therefore in this study, we evaluated the relation between the occurrence of paroxysmal atrial fibrillation and the occurrence of fragmented atrial activity in patients with sick sinus syndrome.

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## METHODS

Eighteen patients with sick sinus syndrome were studied. Twelve patients had a history of paroxysmal atrial fibrillation (group A), while the other six patients had no atrial fibrillation (group B). All patients had evidence of sinus node dysfunction (prolonged corrected sinus node recovery time of more than 550 msec and/or prolonged asystole of more than 4000 msec). Spontaneous occurrence of paroxysmal atrial fibrillation was confirmed using 24 hour Holter monitoring a minimum of two times and by bedside ECG monitoring for 5 days. The patients had neither significant valvular disease nor overt congestive heart failure. We excluded cardiac sarcoidosis and cardiac amyloidosis from this study. The patients were in sinus rhythm at the time of the electrophysiological study.

A-6-F quadripolar electrode catheter (in-

Table 1. Results of sick sinus syndrome patients with paroxysmal atrial fibrillation

Group A

| Pt No | Age/Sex (Y.O) | LAD (mm) | PCWP (mmHg) | Threshold (V) | FAZ (msec) | ERP (msec) | RAR | SNRT (msec) |
|---|---|---|---|---|---|---|---|---|
| 1 | 65 F | 28 | 9.2 | 1.5 | 20 | 240 | (+) | 3250 |
| 2 | 69 F | 43 | 4.4 | 1.5 | 60 | 240 | (+) | 4200 |
| 3 | 78 F | / | 7.0 | 2.0 | 80 | 240 | (+) | 5300 |
| 4 | 72 F | 37 | 9.6 | 1.0 | 0 | 380 | (−) | 3880 |
| 5 | 69 F | 43 | 9.2 | / | 0 | 260 | (+) | 6830 |
| 6 | 79 M | / | 6.8 | 1.5 | 20 | 260 | (−) | 4300 |
| 7 | 66 M | 30 | 6.0 | 1.5 | 40 | 380 | (−) | 2650 |
| 8 | 74 F | / | / | 2.0 | 20 | 240 | (+) | 1140 |
| 9 | 77 M | 28 | 6.0 | 1.5 | 60 | 280 | (+) | 1860 |
| 10 | 46 F | 26 | 6.8 | 2.0 | 80 | 200 | (−) | 6050 |
| 11 | 75 M | 30 | 7.2 | 1.0 | 60 | 280 | (−) | 2445 |
| 12 | 89 M | 25 | 8.0 | 1.5 | 60 | 260 | (+) | 3160 |
| Mean±1SD | 72±10 | 32±7 | 7.3±1.5 | 1.5±0.3 | 43±27 | 272±53 | | 3755±1623 |

abbreviations: Pt=patient, LAD=left atrial dimension, PCWP=pulmonary capillary wedge pressure, FAZ=zone of fragmented atrial activity, ERP=effective refractial period of right atrium, RAR=repetitive atrial response, SNRT=sinus node recovery time, F=female, M=male.

terelectrode distance of 10 mm) was inserted into the high right artium via the femoral vein. Atrial stimulation was performed by the distal pair of electrodes. Stimuli with an intensity of twice the stimulation threshold and a pulse duration of 2 msec, were delivered by a cardiac electrical stimulator (Fukuda Denshi, Model BC 02A). Sinus node recovery time was calculated after 30 sec of atrial overdrive pacing at a pacing rate of up to 210 beats/min. After every eighth paced beat (A1), at the longest pacing cycle length possible, an extra-stimulus (S2) was applied at coupling intervals, decreasing gradually by 20 msec decrement starting from the basic pacing interval until atrial refractoriness was achieved.

Atrial electrograms were recorded by the proximal pair of electrode catheters positioned at the high right atrium. The atrial fragmentation was defined as widening of the atrial activity during the atrial extra-stimulus test reaching more than 150% of that recorded during basic beats[2]. The zone of fragmented atrial activity was defined as the range of S1–S2 intervals at which the fragmented atrial activity occurred. The recording was also made for His bundle electrograms, right ventricular electrograms and three surface electrograms simultaneously at paper speed of 50 mm/sec. We also estimated the stimulation threshold and the effective refractory period of the right atrium. We measured the left atrial dimension by ultrasonic cardiogram as well as the pulmonary capillary wedge pressure.

All values were expressed as mean ± one standard deviation. The statistical significance of differences was analyzed by the non-paired T-test. A p-value of less than 0.05 was considered statistically significant.

Table 2. Results of sick sinus syndrome patients without paroxysmal atrial fibrillation

Group B

| Pt No | Age/Sex (Y.O) | LAD (mm) | PCWP (mmHg) | Threshold (V) | FAZ (msec) | ERP (msec) | RAR | SNRT (msec) |
|---|---|---|---|---|---|---|---|---|
| 1 | 80 F | / | 8.1 | 1.5 | 0 | 320 | (−) | 3060 |
| 2 | 71 F | 20 | / | 1.5 | 0 | 340 | (−) | 4400 |
| 3 | 68 F | 18 | 5.0 | 1.0 | 0 | 320 | (−) | 4740 |
| 4 | 84 F | / | 15.0 | / | 0 | 320 | (−) | 4300 |
| 5 | 36 F | 33 | 8.0 | 1.5 | 80 | 220 | (−) | 1800 |
| 6 | 75 F | 30 | 8.0 | 1.0 | 0 | 300 | (−) | 4600 |
| Mean±1SD | 69±16 | 26±6 | 8.8±3.3 | 1.3±0.2 | 13±30 | 303±39 | | 3817±1055 |
| P value (comparison with group A) | NS | NS | NS | NS | NS | NS | | NS |

abbreviations: same as table 1, NS=not significant.

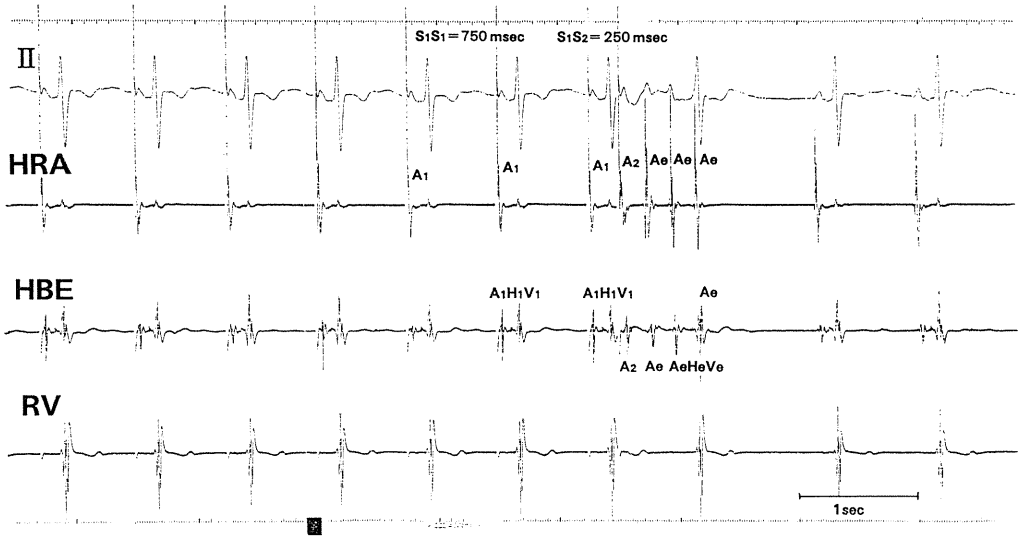


Fig. 1. Atrial electrogram recording from patient 8 in group A. The basic pacing cycle length was 750 msec. The extra-stimulus was delivered in a coupling interval of 250 msec. There was fragmented atrial activity (A2) at HRA, and repetitive atrial response (Ae). HRA=high right atrium, HBE=His bundle electrogram, RV—right ventricle.

## Results

Table 1 and 2 show the results of each group. The left atrial dimension and the zone of the fragmented atrial activity had a tendency to be greater in group A than group B (32±7 mm versus 26±6 mm; 43±27 msec versus 13±30 msec, respectively).

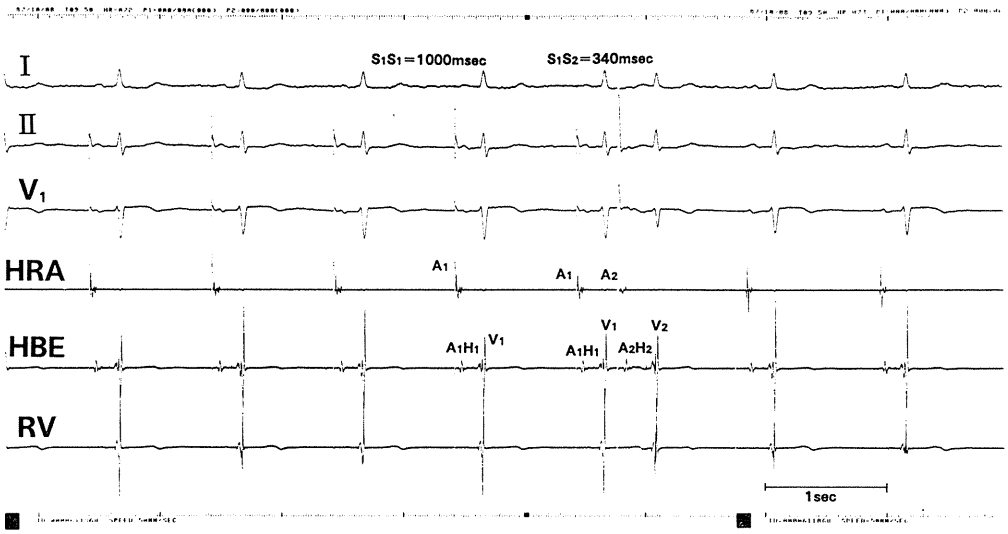


Fig. 2. Atrial electrogram from patient 3 in group B. The extra-stimulus of 340 msec was carried out, but there was no fragmented atrial activity.

Table 3. The ratio between atrial fibrillation and and fragmented atrial activity (A) and the ratio between atrial fibrillation and repetitive atrial response (B)

A

| | FAA (+) | FAA (−) |
|---|---|---|
| Group A | 10 cases | 2 cases |
| Group B | 1 case | 5 cases |

B

| | RAR (+) | RAR (−) |
|---|---|---|
| Group A | 7 cases | 5 cases |
| Group B | 0 | 6 cases |

abbreviation: FAA=fragmented atrial activity, RAR=repetitive atrial response.

The effective refractory period of the right atrium tended to be shorter in group A than group B (272±53 msec, 303±39 msec). These values, however, were not significantly different. The mean ages, the pulmonary capillary wedge pressures, the stimulation thresholds, and the sinus node recovery times shown in Table 1 and 2, and indicate that there were no significant differences between group A and group B.

Figure 1 shows the fragmented atrial activity resulting from an atrial extra-stimulus of patient 8 in group A. After basic pacing at the cycle length of 750 msec, the extra-stimulus was delivered in a coupling interval of 250 msec. There was fragmented atrial activity (A2) at the high right atrium. In this case there were repetitive atrial responses (Ae) at the right atrium and His bundle electrogram. The fragmented atrial activity was found in 10 of the 12 patients (83%) in group A. All patients except one (17%) in group B had no fragmented atrial activity (Figure 2, Table 3). The repetitive atrial response was found in 7 of the 12 patients (51%) in group A, but was not found in group B (Table 3). Fragmented atrial activity showed a sensitivity of 83%, a specificity of 71% and a predictive value of 83% for the occurrence of spontaneous paroxysmal atrial fibrillation. The sensitivity, the specificity and the predictive value of the repetitive atrial response for predicting spontaneous paroxysmal atrial fibrillation were 51%, 56% and 72% respectively. Each value was greater in the fragmented atrial activity than the repetitive atrial response.

## Discussion

We evaluated whether fragmented atrial activity is an appropriate predictive index of spontaneous atrial fibrillation in patients with sick sinus syndrome. The measurement of minimal current strength of extra-stimulus which initiates atrial fibrillation is a classic method in experimental study[3]. Repetitive atrial responses have been utilized as an index of atrial vulnerability in clinical studies[4], but some investigators have reported that repetitive atrial responses are nonspecific[2),5].

The mechanism generating fragmented atrial activity is not known. In recurrent ventricular tachycardia, slow fragmented activity has often been reported by endocardial mapping[6]. Using a chronically infarcted dog model, fragmentation and slowing of conduction have been demonstrated using the premature ventricular stimulation method[7,8]. Buxton *et al.*[9] reported that intraatrial conduction delay in response to a premature stimulus is seen more commonly in patients with spontaneous paroxysmal atrial fibrillation. Similar to the mechanism responsible for fragmented ventricular activity, fragmented atrial activity, in response to premature stimulation, may represent local, continuous and delayed activity. Ohe *et al.*[2] reported that the zones of fragmented atrial activity were wider in patients with spontaneous paroxysmal atrial fibrillation than patients without such dysrythmias. In the present study, the zones of fragmented atrial activity are not as wide as those reported by Ohe *et al.* One reason for the different results may be that they performed the atrial stimulation using a bipolar electrode catheter and recorded the atrial activity using another bipolar electrode catheter, whereas we used a quadripolar electrode catheter for stimulation and recording. Thus, they might have recorded the atrial activity close to stimulation site of the right atrium. This might be a reason for wide fragmented atrial activity zones reported by Ohe *et al*[2].

In this study, fragmented atrial activity was recorded in 10 of the 12 patients (83%) in group A and only 1 of the 6 patients (17%) in group B. An earlier premature stimulation could produce intraatrial conduction delay due to the relative refractory period and/or the asynchronous refractory period of the atrium. Patient 4 and 5 in group A had no fragmented atrial activity. The effective refractory period of patient 4 was 380 msec, the longest in group A, but

the effective refractory period of patient 5 was not so long, 260 msec. In group B, patient 5 was the only one who had fragmented atrial activity and the effective refractory period of patient 5 was the shortest, 220 msec. The early premature stimulation could not excite the atrium because of the long effective refractory period. Furthermore the fragmented atrial activity might not be recorded. However the average effective refractory period of the right atrium was not significantly shorter in group A than group B.

One disadvantage of this study is that we might underestimate the occurrence of spontaneous paroxysmal atrial fibrillation. An episode of paroxysmal atrial fibrillation might have been recorded in patient 5 in group B with further ECG monitoring.

The sensitivity, the specificity and the predictive value of the fragmented atrial activity were greater than those of the repetitive atrial response for predicting spontaneous paroxysmal atrial fibrillation (83%, 71%, 83%; 51%, 56%, 72% respectively). Thromboembolism is a serious complication of sick sinus syndrome, especially with those patients having paroxysmal atrial fibrillation[1]. Thus demonstration of fragmented atrial activity may provide an important clinical index to predict the subsequent occurrence of spontaneous paroxysmal atrial fibrillation. We may be able to prevent thromboembolism by preventing atrial fibrillation or by using anticoagulant therapy for sick sinus syndrome patients demonstrating fragmented atrial activity in the clinical electrophysiologic study.

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