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Dynamic Electrocardiography is Useful in the Diagnosis of Persistent Atrial Fibrillation Accompanied with Second-Degree Atrioventricular Block

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Background: Periodic electrocardiography (ECG) at every clinical visit is generally performed for heart rhythm surveillance, and 24-h Holter ECG is usually used as the gold standard. We aimed to investigate the electrocardiographic features of persistent atrial fibrillation (AF) accompanied with second-degree atrioventricular block (AVB).

Methods: From October 2012 to November 2015, 204 patients with an RR interval > 2.0 s before radiofrequency ablation were included. Dynamic ECG (DCG) was performed before and after the radiofrequency ablation. The patients were divided into two groups based on changes in DCG after radiofrequency ablation: group A (non-second-degree AVB group) and group B (second-degree AVB group). An RR interval > 2.0 s, the distribution of escape rhythm, mean heart rate and the long RR interval in the two groups were analyzed.

Results: After radiofrequency ablation, all 204 patients who had persistent AF converted to sinus rhythm successfully. In group A (n = 193), the distribution of an RR interval > 2.0 s and escape rhythm were significantly correlated with sleep or rest, while no correlation was observed in group B (n = 11). The average RR interval prolongation and escape rhythm were significantly higher in group B than in group A ($p < 0.05$). The average number of long RR intervals > 3.0 s and average number of escape rhythm episodes (< 35 bpm) were significant predictive factors of second-degree AVB after radiofrequency ablation.

Conclusions: DCG is a useful tool for the diagnosis of persistent AF accompanied with second-degree AVB.

Key Words: Atrial fibrillation • Long RR interval • Second-degree atrioventricular block

INTRODUCTION

Atrial fibrillation (AF) is the most common of all cardiac arrhythmias, accounting for nearly one third of all hospital admissions.[1] AF is associated with a decreased quality of life, increased thromboembolic events, and increased rates of death.[2] Periodic electrocardiography (ECG) at every clinical visit is generally performed for heart rhythm surveillance, and 24-h Holter ECG is usually used as the gold standard.[3] However, it may not be adequate for accurate heart rhythm surveillance due to the limited recording duration.[4] Atrioventricular (AV) block is one type of bradyarrhythmia, and common causes include ischemic heart disease, various drugs (e.g., digitalis and calcium channel blockers), connective tissue disorders, and rheumatic fever.[5,6] Bradycardia is defined as a heart rate below the lowest normal value for age. Although less common in children than adults, it can occasionally cause significant morbidity and sudden cardiac death.[7] The risk of death in untreated children with

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complete block of the AV node is 5-8%.[8] Therefore, it is important to identify children at risk and who might benefit from therapeutic interventions.

Second-degree AV block does not usually present with any symptoms, and it can occur in normal children and young adults or athletes.[9,10] However, it is also associated with an underlying heart disease such as intrinsic AV nodal disease, structural cardiomyopathy, myocarditis, endocarditis, acute inferior myocardial infarction, post cardiac surgery, ablation or catheterization procedures and secondary to hypothyroidism or hyperthyroidism.[11] Impaired AV conduction is also a recognized adverse reaction of digitalis, calcium channel blockers, amiodarone, adenosine and β-blockers.[11]

Whether or not AF is accompanied with second-degree AV block has clinical significance for the diagnosis of the patient's condition, drug intervention and treatment guidance. AF associated with AV block is more likely to induce thrombosis and thromboembolic events as well as heart failure and myocardial ischemia due to a slow ventricular rate and electrical remodeling.[12] Therefore, it is very important to establish a standard of diagnosis of AF with second-degree AV block, especially dynamic ECG (DCG).

Due to the disappearance of a sinus P wave during AF, the diagnosis of AF combined with AV block becomes more difficult. The electrocardiographic diagnosis of AV block is currently a challenge for health care professionals who monitor cardiac rhythm. Much of the difficulty is a consequence of differing definitions of the "degree" of AV block in the literature, especially surrounding second-degree AV block. The diagnostic criteria of AF combined with second-degree AV block are unclear, and some scholars have proposed a number of reference standards.[13] However, to date, the ECG diagnostic criteria of AF accompanied with second-degree AV block have not yet been explored. This study was designed to explore the electrocardiographic features of AF accompanied with second-degree AVB.

MATERIALS AND METHODS

This study was approved by the Ethics Committee of our hospital, and informed consent was obtained from each patient. From October 2012 to November 2015, 204 persistent AF patients with an RR interval > 2.0 s before radiofrequency ablation were included in this study. Assessments of structural heart disease included medical history, physical examination as well as 12-lead conventional ECG, and 24-h DCG and echocardiography. Patients with atrial thrombosis, chronic obstructive pulmonary disease and cardiac dysfunction (New York Heart Association (NYHA) Class III or above) were excluded.

Methods

Twenty-four-hour DCG (CT-08, Hangzhou Baihui Medical Equipment Co., Ltd, Hangzhou, China) was performed before and after radiofrequency ablation using a Carto 3 system (Johnson & Johnson, New Jersey, USA). Electrocardiographic evaluation was performed by experienced operators. The mean heart rate, number of RR intervals > 2.0 s and > 3.0 s, the total number and distribution of escape rhythm (including junctional escape and ventricular escape) ≥ 3 times were recorded. The incidence of second-degree AV block after cardioversion was analyzed. The patients were divided into two groups according to the results of DCG after surgery: patients without second-degree AV block (group A), and patients with second-degree AV block (group B).

Statistical analysis

Quantitative data were expressed as means ± standard deviation (SD) and compared using the Student's t-test. Qualitative data were expressed as numbers or percentages and compared using the χ^2 test. Statistical analysis was performed using SPSS 17.0 software (SPSS Inc., Headquarters, Chicago, IL, USA). A p value < 0.05 was considered to be statistically significant.

RESULTS

Between October 2012 and November 2015, 121 males and 83 females with an RR interval > 2.0 s before radiofrequency ablation were included in this study. A typical DCG image before radiofrequency ablation is shown in Figure 1A. After radiofrequency ablation, DCG showed that all AF patients converted to sinus rhythm (Figure 1B). Among the 204 patients, 193 did not have second-degree AV block (group A), and the remaining 11 patients had second-degree AV block (group B). The

demographic data of the patients in the two groups are shown in Table 1.

In group A, there were a total of 1904 (9 times/patient/day) incidences of an RR interval > 2.0 s, of which 19 patients had a total of 53 (3 times/person/day) episodes of an RR interval > 3.0 s, and 27 patients had a total of 246 (9 times/patient/day) episodes of escape rhythm. In group B, there were a total of 319 (29 times/person/24 h) episodes of an RR interval > 2.0 s, of which 5 patients had a total of 45 episodes (9 times/patient/day) of an RR interval > 3.0 s, 6 patients had a total of 102 episodes (18 times/patient/day) of an escape rhythm (escape rhythm < 35 bpm in 5 cases).

The baseline data of the patients in group A are

Table 1. Comparison of the baseline data between the two groups

Item	Group A (n = 193)	Group B (n = 11)
Age (years)	63.4 ± 23.5	64.4 ± 7.9
Gender (male/female)	113/80	8/3
BMI (Kg·m^{-2})	26.2 ± 3.8	26.8 ± 3.1
Complications		
Hypertension (n, %)	81, 42.0%	8, 72.7%
Coronary heart disease (n, %)	47, 24.4%	5, 45.5%
Simple hyperthyroidism (n, %)	9, 4.7%	0, 0%
Rheumatic heart disease (n, %)	2, 1.0%	1, 9.1%
Cardiomyopathy (n, %)	2, 1.0%	0, 0%
Mean ventricular rate (BPM)	74.1 ± 35.7	71.3 ± 8.2

BMI, body mass index; BPM, beats per minute; Group A, non second-degree AVB group; Group B, second-degree AVB group.

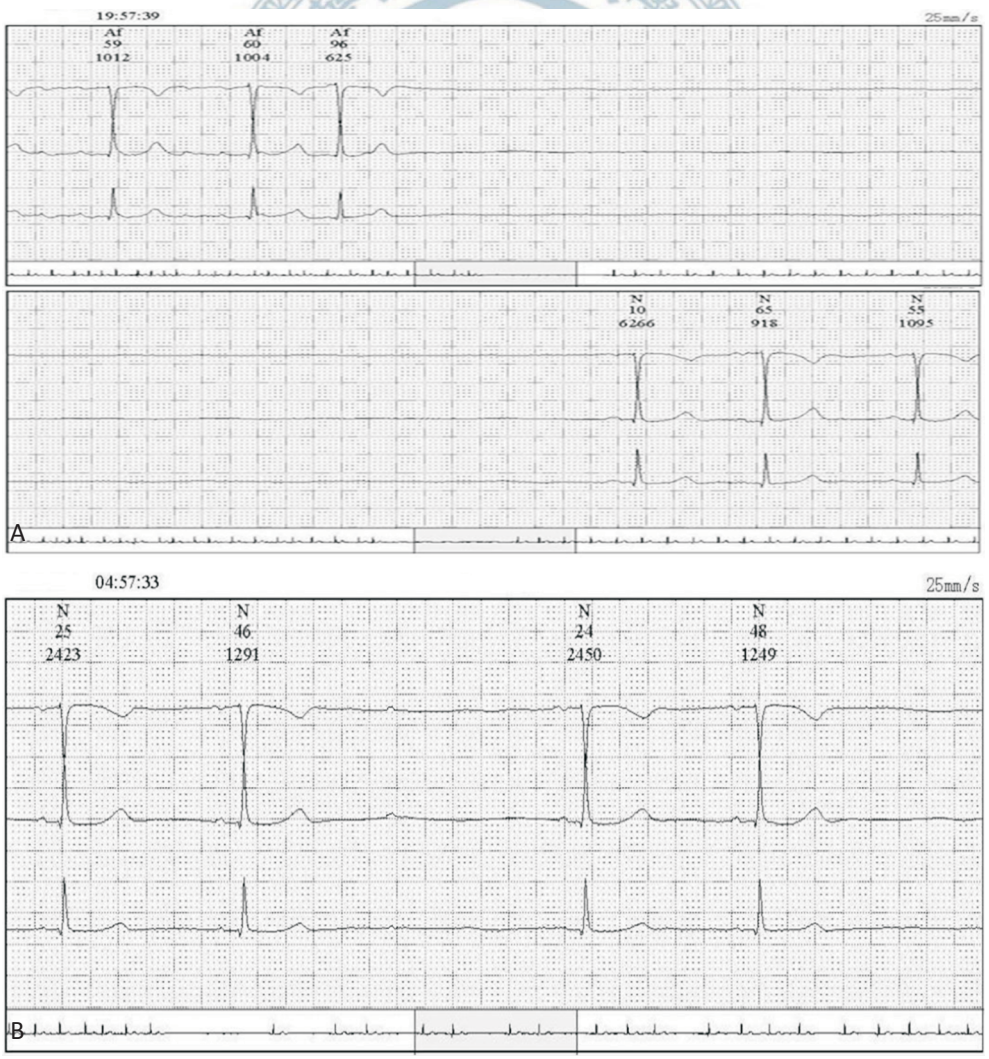

Figure 1. *(A) Typical DCG image before radiofrequency ablation; (B) After radiofrequency ablation, DCG showed that atrial fibrillation converted to sinus rhythm.*

listed in Table 2. There were 8 males and 3 females. Three cases had chest tightness, 3 cases had dizziness, 4 cases had palpitations, and 1 case had syncope.

The mean heart rate and average number of long RR intervals and escape rhythm in the two groups are listed in Table 3. The average number of long RR intervals > 2.0 s (29.7 ± 13.8 vs. 9.2 ± 5.8) and long RR intervals > 3.0 s (9.5 ± 2.2 vs. 3.0 ± 0.8) in group B were significantly higher than those in group A. A higher average number of escape rhythm episodes and the total number of escape rhythm episodes (< 35 bpm) were observed in group B ($p < 0.05$).

As shown in Figure 2A, an RR interval > 2.0 s exhibited a circadian rhythm of double peak values between 11 am and 2 pm and 2 am and 5 am, respectively; while the lowest values occurred between 5 pm and 8 pm in group A and group B, respectively. There was a significant difference between the frequency of an RR interval > 2.0 s between group A and group B during 24-h ECG monitoring ($p < 0.05$). As shown in Figure 2B, the escape rhythm in group A exhibited a circadian rhythm of double peak values between 11 am and 2 pm and 2 am to 5 am, respectively; while the lowest value was observed between 2 pm and 5 pm. In group B, two peak values were observed between 8 am and 11 am and 2 am and 5 am, and the lowest value occurred between 5 pm and 8 pm (Figure 2B). An escape rhythm occurred more frequently in group A compared to group B ($p < 0.05$).

Multivariate analysis showed that the average number of long RR intervals > 3.0 s [odds ratio (OR) 2.14, 95% confidence interval (CI) 1.24 to 3.06; $p = 0.02$] and average number of escape rhythm episodes (< 35 bpm) (OR 3.54, 95% CI 1.40 to 3.26; $p = 0.02$) were significant predictive factors of second-degree AV block after radiofrequency ablation (Table 4).

DISCUSSION

AF is the most common sustained cardiac arrhythmia, and it is associated with an increased risk of stroke, heart failure, cognitive dysfunction, impaired quality of life, and substantial health care costs, and it eventually contributes to an increased risk of cardiac and overall

Table 2. Baseline data of patients in group B

No.	Age	Gender	Symptom	Clinical diagnosis	Mean heart rate (BPM)	R-R interval > 2.0 s	Longest R-R interval (s)
1	63	M	Chest tightness	Hypertension	76	18	2.5 (23:43)
2	69	F	Dizzy	Hypertension	64	48	3.9 (01:18)
3	49	M	Palpitation	Rheumatic heart disease	88	11	2.2 (02:40)
4	54	M	Palpitation	Coronary heart disease	77	28	3.3 (10:25)
5	64	M	Syncope	Hypertension + coronary heart disease	57	54	7.1 (05:13)
6	75	F	Chest tightness	Hypertension	73	31	3.5 (05:33)
7	66	M	Palpitation	Hypertension + coronary heart disease	78	17	2.7 (20:18)
8	65	M	Dizzy	Hypertension	70	25	5.1 (22:57)
9	72	M	Palpitation	Coronary heart disease	68	39	3.5 (18:16)
10	74	F	Dizzy	Hypertension + coronary heart disease	62	42	4.8 (01:34)
11	57	M	Chest tightness	Hypertension	71	14	2.3 (08:41)

BPM, beats per minute; group B, second-degree AVB group.

Table 3. The mean heart rate and the average number of long R-R intervals and escape rhythm in the two groups

Item	Group A (n = 193)	Group B (n = 11)
Mean heart rate (BPM)	74.1 ± 35.7	71.3 ± 8.2
Average number of long R-R intervals > 2.0 s	9.2 ± 5.8	29.7 ± 13.8*
Average number of long R-R intervals > 3.0 s	3.0 ± 0.8	9.5 ± 2.2*
Average number of escape rhythm	9.8 ± 2.2	18.3 ± 5.8*
Average number of escape rhythm (< 35 BPM)	2.1 ± 0.7	10.4 ± 6.9*

BPM, beats per minute; Group A, non second-degree AVB group; Group B, second-degree AVB group. * $p < 0.05$.

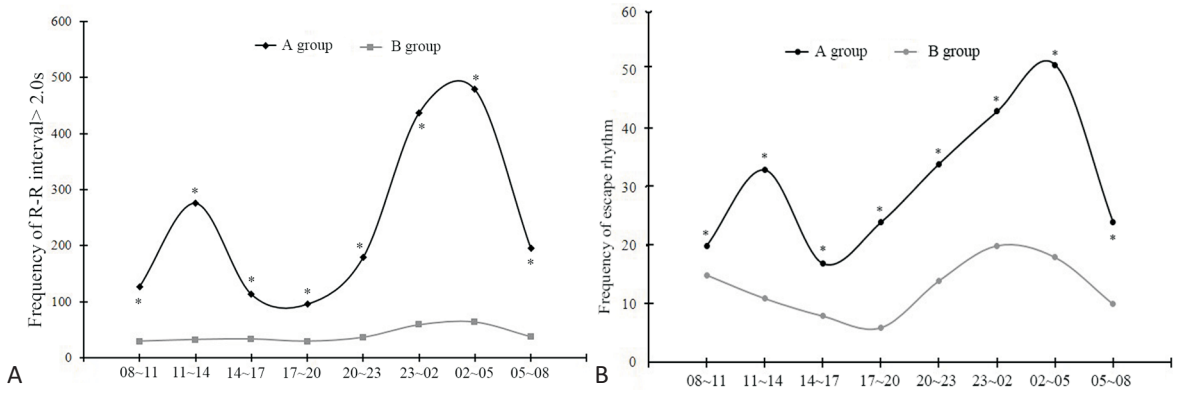

Figure 2. *(A) 24-hour distribution of R-R interval > 2.0 s in group A and group B, * p < 0.05; (B) 24-hour distribution of escape rhythm in group A and group B, * p < 0.05.*

Table 4. Multivariate analysis of the predictive parameters of 2nd AV block in patients with AF

Item	OR	95% CI	p
Age (years)	0.98	0.91-1.09	0.64
Gender	0.70	0.28-1.70	0.39
BMI	1.48	0.86-3.47	0.12
Mean heart rate (BPM)	1.01	0.97-1.10	0.85
Average number of long R-R intervals > 3.0 s	2.14	1.24-3.06	0.02*
Average number of escape rhythm (< 35 BPM)	3.54	1.40-3.26	0.02*

BPM, beats per minute; CI, confidence interval; OR, odds ratio. * p < 0.05.

mortality.[14-17] Several important factors contribute to the risk of developing AF, including structural remodeling (atrial fibrosis), electrical remodeling (dysregulation of I_{Kr}, $I_{K\text{-}Ach}$, and I_{CaL}), abnormal intracellular calcium handling, and neurohormonal alterations (shortening of the refractory period).[18] Second-degree AV block was first described in 1899 by the Dutch physician Karel Frederik Wenckebach by analyzing venous pulsations. Twenty-five years later, after the invention of ECG, Woldemer Mobitz further classified second-degree AV block as type I or II.[19,20] Second-degree AV block remains poorly understood despite major advances in cardiac electrophysiology in the past 3 decades.[13,21-24]

To the best of our knowledge, the ECG diagnostic criteria of AF accompanied with second-degree AV block have not been explored, and no previous study has explored the predictive parameters of second-degree AV block after radiofrequency ablation. Therefore, we conducted this study to investigate the electrocardiographic features of AF accompanied with second-degree AVB. We suggest that AF combined with sleep-related long RR intervals and escape rhythm may not be able to diagnose AF with second-degree AV block. AF accompanied with second-degree AV block should be considered when patients have an obviously increased number of RR intervals > 2.0 s, and the emergence of RR intervals > 3.0 s and escape rhythm (< 35 bpm) which has nothing to do with sleep or rest.

Our study indicated that the average number of long RR intervals > 3.0 s and average number of escape rhythm episodes (< 35 bpm) were significant predictive factors of second-degree AV block after radiofrequency ablation. The results of the current study may provide some reference for the diagnosis of AF accompanied with second-degree AV block. Several possible mechanisms may account for the pathogenesis of AF combined with a long RR interval and escape rhythm. First, occult conduction in the junction area. Second, tension level of the vagus nerve. The results of ambulatory ECG monitoring in the patients with AF showed that a slow ventricular rate occurred during the patient's sleep, and that the probability of a long RR interval and escape rhythm during this period was obviously greater than that in the daytime.[25] This indicates that the change in RR interval in patients with AF is affected by vagus nerve tension. Third, the use of beta blockers. Beta blockers are widely

used clinically, and they can control ventricular rate by inhibiting the conduction of AV node and increasing the likelihood of a long RR interval and escape rhythm.[26] Fourth, digitalis is a commonly used drug for the treatment of heart failure and AF. When the dose is too high, it can induce or aggravate AV block, so that the RR interval becomes prolonged or the escape rhythm slows down. This has important clinical significance with regards to reducing the dosage or with drawing digitalis. Therefore, when assessing the relationship between a long RR interval and AV block, a short RR interval or slow escape rhythm may be due to the above mechanisms rather than actual pathological AV block. Liu et al.[27] also suggested that the heart rhythm in patients with AF changes regularly with exercise and sleep, which suggests that increased vagal tension may lead to a long RR interval. Therefore, in patients with a long RR interval ≥ 3 s, escape rhythm < 35 bpm, and multiple occurrences within 24 h, conduction disorders within the AV junction should be considered.

Arrhythmic episodes occurring during rest or night time are classified as being of vagal origin.[25] In chronobiological analysis, the 24-h distribution showed that an RR interval > 2.0 s and escape rhythm in group A were mainly seen during the rest period from 11 pm to 5 am and 11 am to 2 pm, while the distribution was relatively lower during other time periods, which may be associated with an increase in vagal tone during sleep or rest.[25] In group B, an RR interval > 2.0 s was not only found during the sleep period, but also in sober, activity and other non-sleep time, indicating that an RR interval > 2.0 s is not associated with tension of the vagus nerve.

Several studies have suggested the existence of a link between AF and the autonomic nervous system.[28-30] Exercise-induced AF is considered to depend on sympathetic activation, whereas arrhythmic episodes during rest or at night are classified as being of vagal origin. Yamashita et al.[31] observed different patterns during 24 h, and they reported a double peak of increases in the onset after lunch and at midnight, whereas maintenance showed a sharp decline in the morning when most of the episodes terminated. These findings were interpreted as indirect evidence of a determinant role of vagal mechanisms for AF initiation. A similar conclusion was also inferred by Mitchell et al.[32] who analyzed the onset of atrial tachyarrhythmia in patients with an atrial defibrillator. In this as well as in other studies,[31,32] most the episodes occurred during night time. The chronobiological analysis in the current study is basically consistent with the above research.

In group A, 19 patients had an RR interval > 3.0 s, however only 13 cases had idiopathic AF which was not associated with organic heart disease, while the patients in group B all had organic heart disease. Our findings suggest that AF accompanied with second-degree AV block is associated with organic heart disease, which is consistent with a previous study.[33]

This study has several limitations. First, the retrospective non-randomized design has inherent limitations of such studies. Second, the incidence of second-degree AV block after cardioversion of auricular fibrillation is very low, so the number of patients in group B was relatively lower than those in group A. Therefore, a large-scale study is required to make a more accurate conclusion.

CONCLUSIONS

In conclusion, we suggest that the average number of long RR intervals > 3.0 s and average number of escape rhythm episodes (< 35 bpm) were significant predictive factors of second-degree AV block after radiofrequency ablation. In addition, DCG is a useful tool for the diagnosis of AF accompanied with second-degree AV block.

CONFLICT OF INTEREST

The authors declare that there is no conflicts of interest.

COMPLIANCE WITH ETHICAL STANDARDS

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all subjects included in the study.

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