

# Are Atrial High-rate Episodes a Kind of Sympathetic Overactivity in Patient with Permanent Pacemaker?

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## Abstract

**Objectives:** Atrial high-rate episodes (AHREs) are important cardiac conditions. The purpose of the trial was to assess sympatho-vagal interaction as evaluated by the heart rate variability (HRV) of holter recordings in patients with AHRE.

**Materials and Methods:** All subjects with cardiac devices including dual chamber permanent pacemakers, attending the outpatient pacemaker control units were included. Transthoracic echocardiography and a rest electrocardiogram, and 24-hour Holter monitoring were performed to all patients.

**Results:** One-hundred and fifty subjects were included in this trial. There were 44 patients (29.3%) with AHRE and 106 subjects (70.7%) without AHRE in all population. Standard deviation of all N-N intervals for a selected time period ( $102.1 \pm 30.5$  vs  $124.0 \pm 50.2$ ;  $p=0.008$ ) and normalized power in high-frequency band ( $9.4 \pm 6.6$ ,  $12.7 \pm 7.1$ ;  $p=0.006$ ) were significantly decreased; however, normalized power in low-frequency band ( $28.5 \pm 12.5$ ,  $23.8 \pm 11.6$ ;  $p=0.006$ ) and LF/HF ratio ( $4.71 \pm 3.60$ ,  $2.63 \pm 1.65$ ;  $p<0.001$ ) were significantly increased in AHRE patients.

**Conclusion:** There was a sympathetic overactivity in patients with AHRE. Further studies are needed to demonstrate the role of HRV parameters in AHRE patients.

**Keywords:** Atrial high-rate episodes (AHRE), HRV, autonomic nervous system



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## Introduction

Atrial high-rate episodes (AHREs), known as subclinical arrhythmias, are notable cardiac conditions. Atrial high-rate episode can be described as an episode of faster heart rate, generally higher than 180 beats/minute lasting at least 5 minutes according to the current guidelines<sup>(1)</sup>. AHRE can be recognized by documentation type from atrial fibrillation (AF). AF is detected on an electrocardiogram or Holter monitoring; however, AHREs are merely recorded on a cardiac implantable electronic devices (CIED) read-out<sup>(1)</sup>. The rate of AHRE can reach 50%<sup>(2)</sup>.

Heart rate variability (HRV) has some parameters which represent sympato-vagal interaction of the sinoatrial node (SAN). It is also related to autonomic modulation of SAN. It has been studied to identify the role of autonomic nervous system (ANS) activity in different cardiovascular conditions<sup>(3)</sup>.

The purpose of the trial was to assess sympato-vagal interaction as evaluated by the HRV of Holter recordings in subjects with AHRE.

## Materials and Methods

Patients with CIEDs including dual chamber permanent pacemakers and attending the outpatient pacemaker control unit of three Cardiovascular Centers from March 2010 to February 2019 were enrolled to the study. Patients with heart failure, chronic obstructive pulmonary disease, acute coronary syndrome, previous myocardial infarction, AF, those with decreased ejection fraction (<40%), and those with implantable defibrillator or cardiac resynchronization therapy device were excluded due to heart failure that could impair HRV parameters. We also excluded fulltime pacemaker dependent patients and single-chamber VVI devices. Atrial sensitivity was programmed to 0.5 mV with bipolar sensing.

Clinical assessment, laboratory test, echocardiography and 12 lead electrocardiogram before the Holter recording were done to all subjects.

Ethics committee approval was obtained from University of Health Sciences Turkey, Ankara Keçiören Training and Research Hospital Clinical Researches Ethics Committee (decision no: KAEK2013-18, date: 12.04. 2013).

## Holter Monitoring

CONTEC Holter system was utilized to handle the Holter analysis.

All 24-hour recordings were utilized to assess HRV indexes. Time-domain and spectral results of HRV were calculated using the guideline of ESC<sup>(4)</sup>.

The standard parameters [standard deviation of all NN intervals for a selected time period (SDNN), square root of the mean of the sum of the squares of differences between adjacent RR intervals (RMSSD) and the proportion of differences in successive NN intervals greater than 50 ms (pNN50)] and spectral analysis [high-frequency (HF) component (0.15-0.40 Hz), low-frequency (LF) component (0.04-0.15 Hz)] were used for HRV analysis.

The normalized high-frequency power (HFnu)=100xhigh-frequency power/total power, normalized low-frequency power (LFnu)=100xlow-frequency power/total power, and low/high-frequency power ratio low-frequency power/high-frequency power (LF/HF ratio) were calculated. LF/HF ratio reflects sympatovagal balance (higher 2.5 reflects sympatetic, lower 2.5 reflects parasympatetic overactivity)<sup>(4)</sup>.

## Transthoracic Echocardiography

All subjects underwent transthoracic echocardiography by using a Philips affinity 50 echocardiography machine.

## Statistical Analysis

The Pearson chi-square test, ANOVA and Mann-Whitney U-test were used to compare variables. For post-hoc analysis, the Tukey test was utilized. SPSS 15.0 software was used.

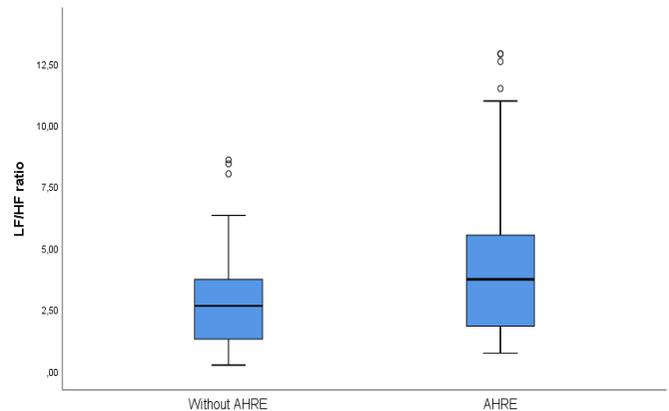
## Results

One-hundred and fifty subjects were included in this trial. Patient characteristics and echocardiography results

are demonstrated in Table 1. There were 44 patients (29.3%) with AHRE and 106 subjects (70.7%) without AHRE in all population. No significant difference was present between two groups in terms of age and gender ratio. Patients with AHRE had increased left atrial diameter and left atrial area, whereas cardiac diastolic functional parameters assessed by mitral valve Continuous Wave Doppler indexes were similar. It was demonstrated in Table 1.

HRV parameters of all subjects were shown in Table 2. SDNN ( $102.1 \pm 30.5$  vs  $124.0 \pm 50.2$ ;  $p=0.008$ ) and HFnu ( $9.4 \pm 6.6$ ,  $12.7 \pm 7.1$ ;  $p=0.006$ ) were significantly lower. LFnu ( $28.5 \pm 12.5$ ,  $23.8 \pm 11.6$ ;  $p=0.006$ ) and LF/HF ratio ( $4.71 \pm 3.60$ ,  $2.63 \pm 1.65$ ;  $p<0.001$ ) were significantly higher in AHRE patients (Figure 1). The alterations in LF

nu and LF/HF ratio showed a higher sympathetic tone and disparity in autonomic activity in AHRE subjects.



**Figure 1.** LF/HF ratio of Subjects with AHRE and without AHRE  
LF: Low frequency, HF: High frequency, AHRE: Atrial high rate episodes

**Table 1.** Baseline characteristics of the patients with AHRE and without AHRE

	AHRE Patients (n=44)	Patients without AHRE (n=106)	p
Age, year	60.4±9.3	58.5±8.4	NS
Gender, M/F (%)	24/20 (54.5/45.5%)	57/49 (53.7/46.3%)	NS
LVEF, %	65.4±4.5	66.3±4.7	NS
Left atrial diameter (cm)	3.7±0.7	3.2±0.4	<b>0.001</b>
Left atrial area (cm <sup>2</sup> )	20.4±3.2	13.1±1.9	<b>&lt;0.001</b>
E peak (m/sec)	0.7±0.1	0.7±0.2	NS
A peak (m/sec)	0.7±0.1	0.8±0.2	NS
E deceleration time (msec)	215±28	217±34	NS
Isovolumic relaxation time (IVRT) (msec)	104±14	103±12	NS

M/F: Male/female, LVEF: Left ventricle ejection fraction, AHRE: Atrial high-rate episodes, NS: Not significant

**Table 2.** HRV parameters in subjects with AHRE and without AHRE

	AHRE subjects	Subjects without AHRE	p
Heart rate	81.2±17.5	73.8±14.2	<b>&lt;0.001</b>
SDNN (ms)	102.1±30.5	124.0±50.2,	<b>&lt;0.001</b>
RMSSD (ms)	40.2±21.2	38.1±19.0	NS
PNN50 (%)	11,7±1,5	10±1,4	NS
24-hour LFnu	28.5±12.5	23.8±11.6	<b>0.02</b>
24-hour HFnu	9.4±6.6	12.7±7.1	<b>0.029</b>
LF/HF ratio	4.71±3.60	2.63±1.65	<b>&lt;0.001</b>

SDNN: Standard deviation of all NN intervals for a selected time period, AHRE: Atrial high-rate episodes, RMSSD: Square root of the mean of the sum of the squares of differences between adjacent RR intervals, PNN50: The proportion of differences in successive NN intervals greater than 50 ms, LFnu: Normalized power in low frequency band, HFnu: Normalized power in high-frequency band

Any correlation could not be found between any HRV parameters and demographic features of the subjects.

## Discussion

In the study, we showed that patients with AHRE had more impaired HRV parameters reflecting sympathetic overactivity compared to those without AHRE. To the best of our knowledge, this is the first study examining HRV parameters in patients with AHRE in preserved LV systolic function.

AHREs are not a rare condition in subjects having intra-cardiac devices without AF after development in cardiovascular follow up. Atrial high-rate episodes can be observed highly in next times. Atrial high-rate episodes are usually thought of similar to clinical paroxysmal AF. It could be given support by former trials showing that AHREs have an increased relation to clinical AF<sup>(5)</sup>.

HRV parameters reflect the autonomic activity on the heart. It is related to alterations in autonomic balance. In the study, the deterioration of both various parameters of HRV in AHRE patients was shown. It has been mentioned that disrupted sympatho-vagal interaction for the good of sympathetic system can be caused by heart repolarization abnormalities and tachyarrhythmias<sup>(6)</sup>.

Several risk factors such as inflammation, autonomic changes, high pressure or volume burden can play roles as potential agents to cause a favorite substrate for AHRE creation<sup>(7)</sup>. Various trials have investigated that different promoting agents to atrial arrhythmias look like autonomic layout. Parasympathetic activation is demonstrated to decrease the atrial effective refractory period and tendency to atrial arrhythmias<sup>(8)</sup>. In some cardiac disorders, sympathetic activity plays a crucial role in atrial arrhythmia initiation<sup>(9)</sup>. In this study, higher sympathetic tone in patients with AHRE was also found.

## Conclusion

There was a sympathetic overactivity in patients with AHRE in the current study. Further larger trials are needed

to demonstrate the role of HRV parameters in AHRE patients.

## Ethics

**Ethics Committee Approval:** This study was approved by University of Health Sciences Turkey, Ankara Keçiören Training and Research Hospital Clinical Researches Ethics Committee (decision no: KAEK2013-18, date: 12.04. 2013).

**Informed Consent:** Informed consent was obtained from all participants.

**Peer-review:** Externally peer-reviewed.

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