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Assessment of cardiac arrhythmias in patients with ankylosing spondylitis by signal-averaged P wave duration and P wave dispersion

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Abstract. – OBJECTIVE: Aortic regurgitation, conduction disturbances, increased myocardial fibrosis and pericarditis could be seen in ankylosing spondylitis (AS). However, less attention has been paid to supraventricular arrhythmias (SVA) and atrial conduction system changes. We aimed to assess SVA and conduction system changes in patients with AS.

PATIENTS AND METHODS: Twenty-eight patients (24 men; mean age, 28.7 ± 5.7 years) with AS and 30 healthy volunteers (26 men; mean age, 29.3 ± 5.8 years) were enrolled. All subjects were evaluated by 24-hour ambulatory electrocardiogram, 12 lead standard electrocardiogram (ECG) for P wave dispersion (Pd), and signal-averaged ECG (SAECG) for P wave duration (SAPWD).

RESULTS: SVAs were detected in 9 patients with AS (32%) and 3 controls (10%; *p* = 0.02). Mean SAPWD (115.7 ± 28.6 ms vs. 100.2 ± 18.7 ms, *p* = 0.017) and mean Pd (11.9 ± 4.8 ms vs. 9.3±3.6 ms, 0.023) was longer in patients with AS than the control group. When patient with AS were divided into 2 subgroups as patients with or without SVA, the Pd (16.2 ± 5.0 *vs.* 9.9 ± 3.2, *p* = 0.001), SAPWD (151.4 ± 7.8 *vs.* 98.7 ± 16.1, *p* = 0.001) and Bath ankylosing spondylitis disease activity index (BASDAI) (5.1 ± 1.6 vs. 3.7 ± 1.0, *p* = 0.014) were significantly greater in the subgroup with arrhythmias compared to the subgroup without arrhythmias. There was a strong positive correlation between BASDAI and SAPWD (r = 0.622, *p* = 0.001). There was also a moderate positive correlation between BASDAI and Pd (r = 0.479, *p* = 0.01).

CONCLUSIONS: SVA were detected more frequently in AS than control group. SAPWD and Pd were prolonged in patients with AS. Clinical severity assessed with BASDAI had a positive correlation with prolongation of SAPWD and Pd.

Key Words:
Ankylosing spondylitis, P wave dispersion, P wave duration, Signal-averaged electrocardiogram, Supraventricular arrhythmias.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial skeleton presented by back pain and progressive stiffness of the spine[1,2]. Patients with AS have an average mortality of approximately 1.5-2 fold that of the general population. Mortality due to cardiovascular disease has been estimated about 20-40%[3]. The cardiac manifestations including aortic regurgitation, conduction disturbances and increased myocardial fibrosis causing abnormalities of left ventricular relaxation and pericarditis could be seen in AS[3-7]. However, supraventricular arrhythmias and atrial conduction system changes have not been fully elucidated.

Signal-averaged P wave duration (SAPWD) and P wave dispersion (Pd) are the commonly used electrocardiographic parameters in clinical cardiology. They can be used for determining patients at risk for the development of atrial arrhythmias. It has been demonstrated that both parameters indicate heterogeneous and discontinuous conduction of sinus impulses within the atrial myocardium in many clinical studies to date[8-10].

In the present study, we aimed to assess the relationship between AS, supraventricular arrhythmias and atrial conduction system changes. For this purpose, we performed a 24-hour ambulatory electrocardiogram, 12 lead standard ECG for Pd, and signal-averaged ECG (SAECG) for SAPWD.

Patients and Methods

Study Population

A total of 28 consecutive patients with AS were included in the study. Patients were regarded as

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having AS if they fulfill the 1984 Modified New York Criteria for AS[1]. This set of criteria consists of a subset of clinical parameters and a subset of radiological parameters. Clinical parameters are; low back pain and stiffness for more than three months that improves with exercise, but is not relieved by rest, limitation of motion of the lumbar spine in both the sagittal and frontal planes, limitation of chest expansion relative to normal values correlated for age and sex. Radiological parameters are; sacroiliitis grade >2 bilaterally, sacroiliitis grade 3 to 4 unilaterally. A patient was regarded as having definite AS if he or she fulfills at least 1 radiological parameter plus, at least, one clinical parameter.

Patients were also evaluated using the Turkish version of the Bath ankylosing spondylitis disease activity index (BASDAI)[11]. The BASDAI consists of a 1-10 scale measuring discomfort, pain, and fatigue (1 being no problem and 10 being the worst problem) in response to six questions asked of the patient pertaining to the five major symptoms of AS. The BASDAI consists of a 1-10 scale measuring discomfort, pain, and fatigue (1 being no problem and 10 being the worst problem) in response to six questions asked of the patient pertaining to the five major symptoms of AS (fatigue, spinal pain, arthralgia or swelling, enthesitis, morning stiffness duration, stiffness duration, morning stiffness, severity). To give each symptom equal weighting, the average of the two scores relating to morning stiffness is taken. The resulting 0 to 50 score is divided by 5 to give a final 0-10 BASDAI score. Patients with diabetes mellitus, chronic renal failure, chronic liver disease, neurologic diseases, structural heart disease, taking medications which have effects on the autonomic system, and smoking habit were excluded from the study.

Thirty volunteers matched for age and sex with no previous history of cardiac disease served as a control group. All patients were in sinus rhythm during the study period. A detailed history and physical examination were obtained in all participants. All subjects underwent ECG, SAECG, 24-hour ambulatory ECG monitoring and transthoracic echocardiography after a detailed medical history, laboratory and physical examination. The study protocol is in accordance with the Declaration of Helsinki and was approved by local Ethics Committee. All patients were given informed consent.

Electrocardiography

Using a General Electric MAC 5000 Resting ECG Analysis System device (GE Marquette Medical Systems Inc., Milwaukee, WI USA), a 12-lead surface ECG and orthogonal derivations, as well as SAECG recordings at a speed of 50 mm/s and 1 mV/cm calibration, were obtained from all subjects in the supine position following 15 minutes of rest. The subjects were asked to breathe normally and not to cough or speak during the recordings. In the ECG recording, following the determination of maximum P wave and minimum P wave duration, Pd was calculated by subtracting these 2 values. Maximum P wave and minimum P wave durations were measured as the distance between the points at which the beginning of the P wave deflection intersected the isoelectric line and the point at which the end of the P wave intersected the isoelectric line using a magnifying lens. Electrocardiography leads at which the beginning or end of the P wave could not be precisely determined were excluded from the analysis. The SAPWD in the SAECG was obtained from the average of at least 250 P waves performed with orthogonal derivations recorded by the MAC 5000 device at a 0.05 μV-0.20 μV noise level and 40-250 Hz band-pass filtering.

24-Hour Ambulatory ECG Monitoring

24-hour ambulatory ECG monitoring was performed on all patients and the control group using an Ela Medical Spider View digital Holter recording system (Ela Medical Corp., Montrouge, France). The data obtained from this 3-channel recording system was digitally evaluated using an Ela Medical Synescope program in terms of the presence of atrial and ventricular arrhythmias. The supraventricular arrhythmias accepted as clinically significant were as follows: frequent atrial premature complexes (APCs; an atrial early beat frequency of ≥ 2000/24 hours), atrial fibrillation (AF), atrial flutter, or other paroxysmal supraventricular tachycardias (i.e., atrioventricular nodal re-entrant tachycardia and atrioventricular re-entrant tachycardias). Ventricular arrhythmias were classified according to the modified Lown criteria[12]. Lown grade ≥ 2 was considered clinically significant.

Transthoracic Echocardiography (TTE)

All patients underwent transthoracic echocardiography. Echocardiographic examination was performed in the left lateral position from parasternal long- and short-axes, and apical two- and four-chamber views. From the parasternal long axis, the left ventricle end-diastolic diameter (LVEDD) and the left ventricle end-systolic di-

ameter (LVESD) were measured using M-mode (at the mitral chordal level perpendicular to the long axis of the ventricle), and then LVEF was calculated. Left atrium and aortic diameters were measured in the parasternal long axis view using M-mode echocardiography in accordance with the American Society of Echocardiography's Guidelines as the distance from the anterior margin to the posterior margin[13].

Statistical Analysis

Distribution of data was assessed by using a one-sample Kolmogorov-Smirnov test. Data are demonstrated as mean ± SD for normally distributed continuous variables and frequencies for categorical variables. For numerical variables, an independent sample *t*-test and Mann-Whitney U test were used for intergroup comparisons. A chi-square test and Fischer's exact chi-square test were used for comparisons of categorical variables. The correlations between BASDAI with SAPWD and Pd were examined with Pearson's correlation analysis. Statistical analysis of the data was conducted using SPSS 15 (SPSS Inc., Chicago, IL, USA) and two-tailed p-value < 0.05 was considered statistically significant.

Results

Patients with AS and control groups were similar with respect to age (28.7 ± 5.7 vs. 29.3 ± 5.8 years), gender distribution ([male/female] 24/4 vs. 26/4), basal heart rate (72.0 ± 8.3 vs. 74.9 ± 9.3 beats/minute), systolic blood pressure (113.0 ± 4.2 *vs.* 114.8 ± 8.4 mmHg), diastolic blood pressure (73.1 ± 9.6 *vs.* 71.8 ± 8.0 mmHg), left atrial diameter (32.1 ± 3.5 mm and 32.8 ± 2.7 mm) and left ventricular ejection fraction (LVEF) (65.7 ± 3.6 vs. 63.8 ± 2.8%). Demographic and clinical characteristics of the groups were summarized in Table I.

All subjects were in sinus rhythm at baseline. The resting ECG was normal in all individuals in the control group. First degree AV-block (PR interval) ≥ 200 ms was diagnosed in 1 patient among AS group. Mean SAPWD (115.7 ± 28.6 ms vs. 100.2 ± 18.7 ms, $p = 0.017$) and mean Pd (11.9 ± 4.8 ms *vs.* 9.3 ± 3.6 ms, 0.023) was higher in patients with AS than the control group (Figure 1). On 24-hour ambulatory Holter monitoring, frequent APCs were noted in 4 patients (14.2%), paroxysmal atrial fibrillation attacks in 3 patients (10.7%), and supraventricular tachycardia attacks in 2 patients (7%) in patients with AS. The number of patients with SVA was 9 (32.1%) in AS (Figure 2). Frequent APCs were noted in only 3 patients (10%) in control group. A statistically significant difference existed between groups in terms of the prevalence of SVA group ($p < 0.001$). All arrhythmias noted in the two groups were of supraventricular origin and no clinically significant ventricular arrhythmias were observed in any of the subjects.

When patient with AS were divided into 2 subgroups as patients with or without SVA, the Pd (16.2 ± 5.0 *vs.* 9.9 ± 3.2, $p = 0.001$), SAPWD (151.4 ± 7.8 *vs.* 98.7 ± 16.1, $p = 0.001$) and BASDAI (5.1 ± 1.6 *vs.* 3.7 ± 1.0, $p = 0.014$) and were significantly greater in the subgroup with arrhythmias

Table I. Demographic and clinical characteristics of the groups.

Variable	AS group (n = 28)	Control group (n = 30)	*p*-value
Age, years	28.7 ± 5.7	29.3 ± 5.8	NS
Gender (M/F)	24/4	26/4	NS
Basal heart rate, bpm	72.0 ± 8.3	74.9 ± 9.3	NS
Left atrial diameter, mm	32.1 ± 3.5	32.8 ± 2.7	NS
LV end-diastolic diameter, mm	46.1 ± 3.7	46.8 ± 3.6	NS
LV end-systolic diameter, mm	31 ± 0.8	32 ± 0.7	NS
LVEF, %	63.8 ± 2.8%	65.7 ± 3.6	NS
SBP, mmHg	113.0 ± 4.2	114.8 ± 8.4	NS
DBP, mmHg	73.1 ± 9.6	71.8 ± 8.0	NS
BASDAI	4.2 ± 1.4	0	< 0.001
P wave dispersion, ms	11.9 ± 4.8	9.3 ± 3.6	0.023
P wave duration, ms	115.7 ± 28.6	100.2 ± 18.7	0.017

Numerical variables with a normal distribution were presented as the mean ± standard deviation. BASDAI: Bath ankylosing spondylitis disease activity index, LV: left ventricle, SBP: systolic blood pressure, DBP: diastolic blood pressure.

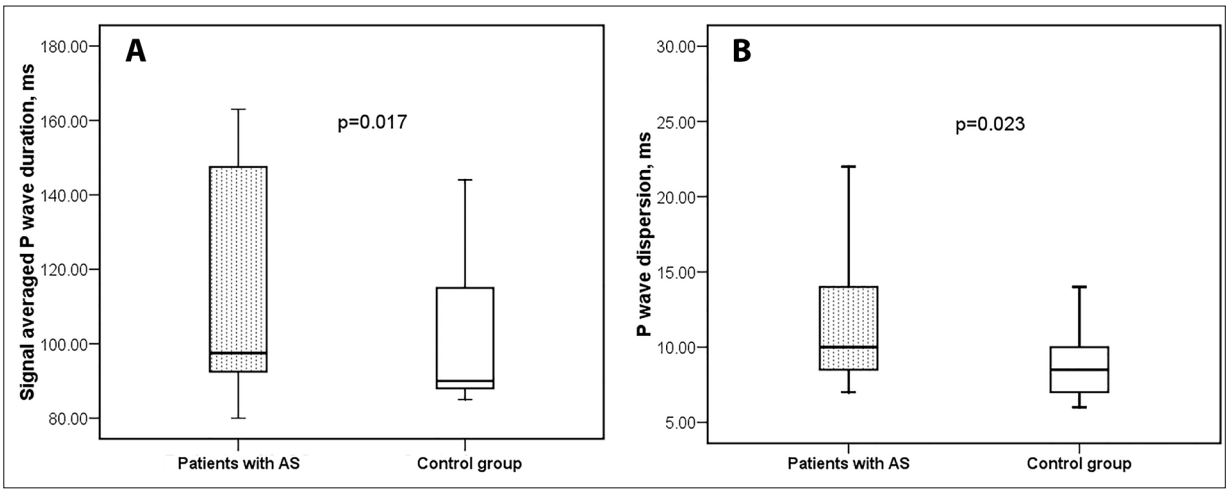

Figure 1. Comparison of **(A)** SAPWD, **(B)** P wave dispersion between two groups.

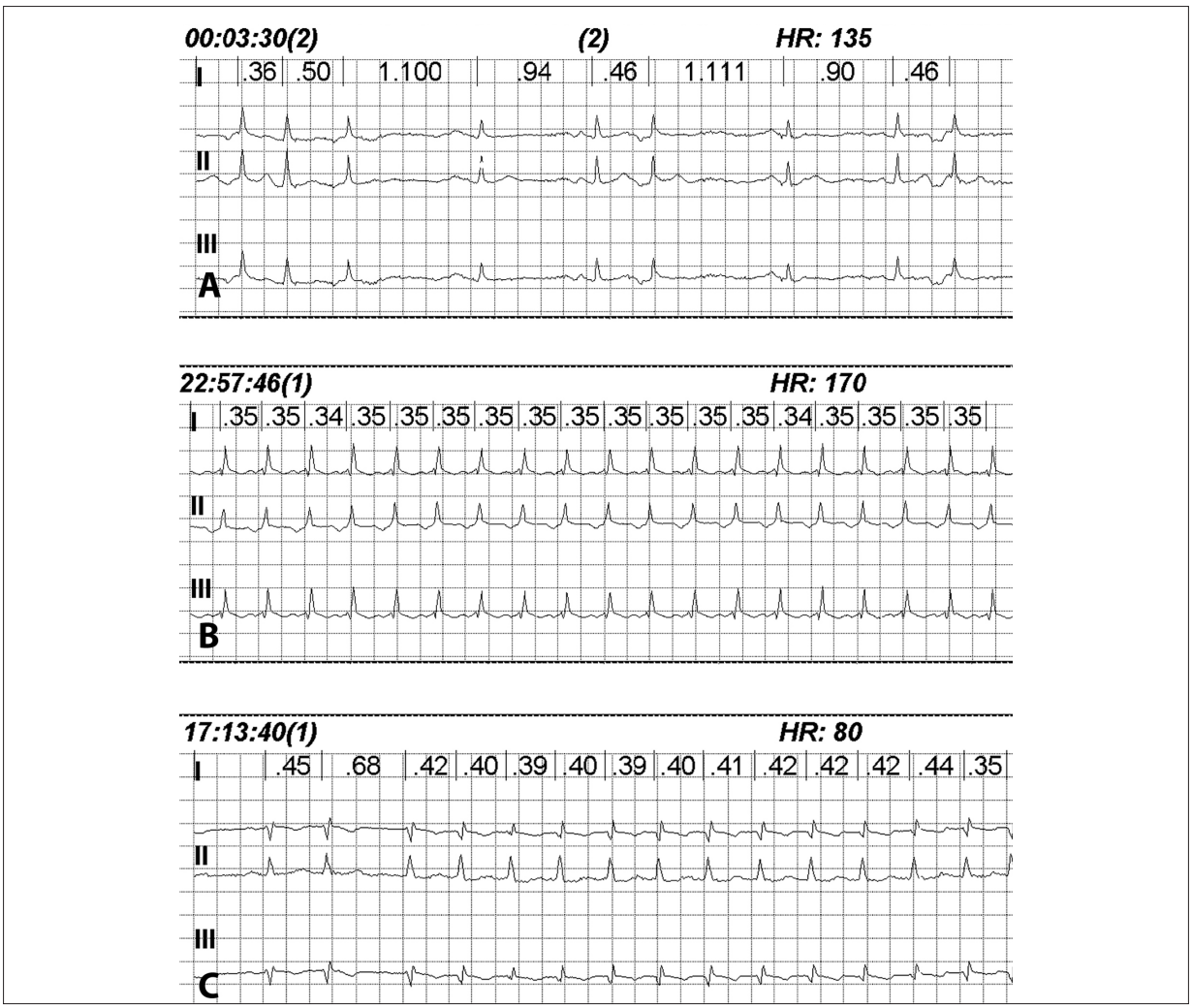

Figure 2. Supraventricular arrhythmias among AS patients. **(A)** Atrial premature contractions, **(B)** supraventricular tachycardia and **(C)** atrial fibrillation.

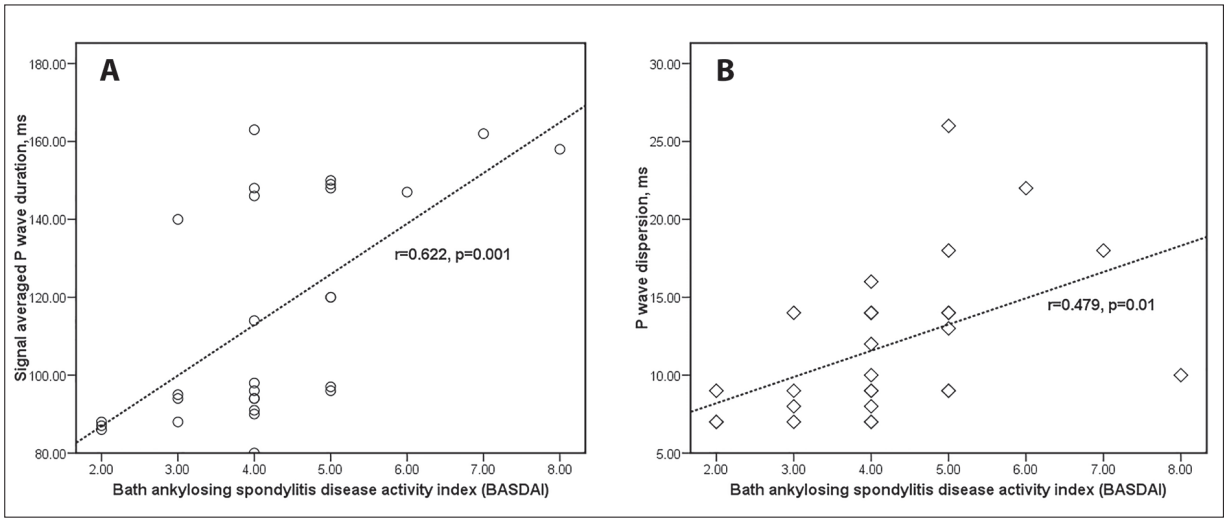

Figure 3. Correlation between BASDAI and **(A)** signal averaged P wave duration (r = 0.622, p = 0.001), **(B)** P wave dispersion (r = 0.479, *p* = 0.01).

compared to the subgroup without arrhythmias. Spearman's correlation analysis revealed a strong positive correlation between BASDAI and SAPWD (r = 0.622, *p* = 0.001). There was also a moderate positive correlation between BASDAI and SAPWD (r = 0.479, *p* = 0.01) (Figure 3).

Discussion

The main findings of the present study are as follows: (1) supraventricular arrhythmias were detected more frequently in AS than control subjects, (2) mean SAPWD and Pd were longer in patients with AS, (3) in arrhythmic subgroup of patients BASDAI, SAPWD and Pd were higher, (4) clinical severity had positive correlation with SAPWD and Pd. To the best of our knowledge, our study is the first to report the presence prolongation of SAPWD in patients with AS. Furthermore, clinical severity assessed by BASDAI had a positive correlation with prolongation of SAPWD and Pd. Furthermore, present study is the first using 3 parameters together in terms of investigating the prevalence and causes of supraventricular arrhythmias and atrial conduction system changes in patients with AS

SAPWD and Pd are the commonly used electrocardiographic parameters in clinical cardiology[8,14]. They can be used for determining patients at risk for the development of atrial arrhythmias. It has been demonstrated that both parameters indicate heterogeneous and discontinuous conduction of sinus impulses within the atrial myocardium in many clinical studies to date[8-10]. It was shown that Pd was prolonged in chronic, inflammatory, and rheumatic diseases such as rheumatoid arthritis, scleroderma and Behçet's disease[15-17].

Cardiac involvement is a well-known complication of AS. Although classically thought of as a spinal and peripheral articular disease, extra-articular organs, such as the eyes, lungs, neurological system and heart can be affected[18-20]. Radford et al[21] reported that patients with ankylosing spondylitis had a greater risk of death relative to the general population. The most frequently seen abnormalities are aortic root disease and conduction system disturbances which can be seen in 5-10% of AS patients[22-25]. In a recent study performed by Forsblad-d'Elia et al[18] ECG abnormalities were common and cardiac conduction system abnormalities were found in 10-33%. In another Dutch study, Dik et al[26] reported associations between the PR interval and age, disease duration, and BMI as well as between the QRS duration and male gender, disease duration and severity. Acar et al[27] reported that atrial electromechanical coupling intervals and Pd were delayed in patients with AS. In our study, supraventricular arrhythmias were more frequent in AS. SAPWD and Pd were prolonged in patients with AS. Importantly, clinical severity assessed with BASDAI had a positive correlation with prolongation of SAPWD and Pd. Limitations of the present study are the relatively small number of patients, and the results are based on a single center.

Conclusions

SVA were encountered frequently in AS. SAP-WD and Pd were prolonged in patients with AS. Clinical severity assessed with BASDAI had a positive correlation with prolongation of SAP-WD and Pd. Cardiac involvement is common in AS and other spondyloarthropathies and ECG is, therefore, suggested to be part of the routine evaluation of such patients, in particular when the patients have symptoms which might be related to cardiac conduction abnormalities and arrhythmias.

Disclosures

The authors have nothing to disclose.

Conflict of Interests

The Authors declare that they have no conflict of interests

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