Acta Medica Alanya

RESEARCH ARTICLE

ARAŞTIRMA

Acta Medica Alanya

2018;2(2):96-101

DOI:10.30565/medalanya.393936

Red Cell Distribution Width and Subclinical Left Ventricular Dysfunction in Patients with Ankylosing Spondylitis

Ankilozan Spondilit Hastalarında Kırmızı Hücre Dağılım Genişliği Ve Subklinik Sol Ventrikül Disfonksiyonu

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ABSTRACT

Aim: The aim of this study is to investigate the relationship between left ventricular function and red cell distribution width (RDW) measured by myocardial performance index in patients with Ankylosing Spondylitis (AS).

Patients and Methods: The study included 35 patients with AS and 38 controls. Control group was consisted of age and gender matched individuals without any cardiologic complaint and systemic disease. Laboratory parameters including RDW tests and transthoracic echocardiographic evaluation were conducted consecutively on the entire cohort of ankylosing spondylitis patients and healthy individuals.

Results: In our study, no statistically significant difference was found between two groups, in terms of general properties such as age, gender, Body Mass Index (BMI), body surface area, systolic and diastolic blood pressure, smoking, serum lipid levels and blood glucose levels. ESR and CRP levels of AS group were found to be significantly higher compared to that of control group. EF and FS, which are among the parameters of systolic function, were normal in all individuals of both groups and there was no significant difference between two groups. However, myocardial performance index (MPI) was higher in patients with AS than in controls. In addition, we showed a significant positive correlation between RDW and MPI (r: 0.372 , p: 0.001).

Conclusion: Myocardial performance index may be useful for the early diagnosis of potential heart failure, by providing an earlier diagnosis of left ventricular dysfunction in patients with ankylosing spondylitis. Also , red cell distribution width was significantly correlated with myocardial performance index in these patients.

Key words: Myocardial performance index, ankylosings pondylitis, red cell distribution

ÖZ

Amaç : Bu çalışmanın amacı Ankilozan spondilit (AS) hastalarında miyokardial performans indeksi ile ölçülen sol ventrikül fonksiyonu ve bunun kırmızı hücre dağılım genişliği (RDW) ilişkisini incelemektedir.

Hastalar ve Yöntem: Çalışma 35 Ankilozan spondilit hastası ve 38 kontrol içermektedir. Kontrol grubu yaş ve cinsiyet açısından eşleştirilmiş, kardiyak ve sistemik hastalığı olmayan kişilerden oluşmaktadır. Hemogram parametrelerini içeren laboratuar testleri ve trans torasik eko kardiografik değerlendirme tüm AS hastalarına uygulandı.

Bulgular: Çalışmamızda yaş, cinsiyet , vücut kitle indeksi , sistolik ve diyastolik kan basıncı , sigara kullanımı, serum lipid ve kan şekeri seviyeleri açısından anlamlı fark saptanmadı. Eritrosit sedimentasyon hızı (ESR) ve CRP seviyeleri ise kontrol grubu ile kıyaslandığında AS grubunda anlamlı olarak yüksek saptandı. Sistolik fonksiyon parametreleri olan EF ve FS tüm çalışma grubunda normal bulundu. Fakat miyokardial performans indeksi (MPI) , AS hastalarında kontrol grubundan daha yüksekti. Ek olarak RDW ve MPI arasında belirgin pozitif korelasyon mevcuttu. (r : 0,372, p = 0,001)

Sonuç: Miyokardial performans indeksi ankilozanspondilit hastalarında, sol ventikül disfonksiyonunda erken tanı sağlayarak potansiyel kalp yetmezliğinin erken teşhisinde kullanılabilir. Ayrıca bu hastalarda RDW miyokardial performans indeksi ile belirgin korelasyon göstermektedir.

Anahtar kelimeler: Miyokardiyal performans indeksi, ankilozan spondilit, kırmızı hücre dağılımı

Received Date:12.02.2018/ Accepted Date:09.03.2018 / Published Date:02.07.2018

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Ankylosing spondylitis (AS) is a chronic, inflamatory and systemicic disease which affects axial skeleton , peripheral joints , eyes , pulmonary system, gastrointestinal system, genitourinary system and cardiovascular system [1,2]. Mortality is 1.6-1.9 fold higher in patients with AS than general population. Main causes of mortality in AS patients are vertebral fractures , pulmonary and renal failure. Some authors suggested that cardiovascular mortality is increased in patients with AS compared to normal population. Aortic insufficiency , conduction disorders, mitral valvular diseases and cardiomyopathy are associated with cardiac mortality and morbidity in patients with AS [3,4]. In the previous studies , echocardiographic reports have showed ventricular dysfunction in AS. Cardiomyopathy may be asymptomatic in the early stages of the disease and may subsequently progress to significant heart failure [5].

Red cell distribution width (RDW) is a marker of variation of the size of circulating red blood cells and has been discovered as a new inflammatuar biomarker in heart failure recently. It was showed that elevated RDW values were associated with increased mortality and morbidity in chronic heart failure [6,7,8]. Red cell distribution width is reported as a part of routine blood cell count done for all patients , admitted with the diagnosis of AS. However the relation between RDW and subclinical left ventricular dysfunction assessed by echocardiography has not been studied before in this population .

The aim of our present study is to analyze functions of left ventricle by using myocardial performance index and evaluate its relationship with RDW in patients with AS.

PATIENTS AND METHODS

According to modified New York Criteria, the study enrolled the patients with AS without having a clinical cardiac complaint. The patients with a history of myocardial infarction , serious valvular disease , atrial fibrillation , diabetes mellitus, hypertension or hypertrophic cardiomyopathy were excluded from the study. Also patients with other autoimmune disease, anemia,other hematologic disease or /and received blood transfusion during the past 6 months, infectious disease, chronic liver or kidney disease were excluded. Control group was consisted of age and gender matched healthy individuals without any cardiologic complaint and systemic disease. All patients and controls were informed about the study and written consents were obtained. The study was approved by local Ethic Committee. In both groups, height, weight, blood pressure and heart rate were measured. As laboratory evaluations, fasting blood glucose levels, total cholesterol (TChol), LDL cholesterol (LDL-Chol), HDL Cholesterol (HDL-Chol), triglyceride (TG) levels, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and hemogram values and red cell distribution width(RDW) values as a component of complete blood count were examined.

The patients were evaluated using Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), Bath ankylosing spondylitis metrology index (BASMI), Maastrich ankylosing spondylitis enthesitis score (MASES), ankylosing spondylitis quality of life questionnaire (ASQoL) [9,10].

To evaluate the heart rate, rhythm, conduction defects and myocardial ischemia, all cases had standard 12-lead electrocardiogram (ECG) following a 15-minute resting period and they underwent a treadmill exercise test using Full Vision inc. 3017 Full Vision Drive Newton, USA device according to standard Bruce protocol. In ECG and treadmill exercise test, individuals with cardiac pathology were excluded from the study. Transthoracic echocardiography and M-mode, two dimensional and colored Doppler echocardiography (Vivid 7 Dimension, GE Vingmed Ultrasound Horten, Norway) examinations were performed using a probe with a frequency of 4 MHz, according to the recommendations of American Echocardiography Society [11].

In the echocardiography, aortic root diameter (ARD), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), ejection fraction (LVEF), fractional shortening (FS), interventricular septum diastolic thickness (IVSDT), left atrium diameter (LAD), Mitral E wave velocity (E), Mitral A wave velocity (A) , Ejection time (ET), isovolemic relaxation time (IRT) and isovolemic contraction time (ICT) were measured. Left ventricular function was evaluated by using LVEF, FS and myocardial performance index (MPI). Myocardial performance index of the LV was obtained by dividing IRT and ICT to ET (Figure 1). Myocardial performance index is considered as the sum of an index reflecting systolic function and an index reflecting diastolic function. In

this study , MPI expresses global LV function , while other echocardiographic parameters are limited to reflect mainly either LV systolic or diastolic function.

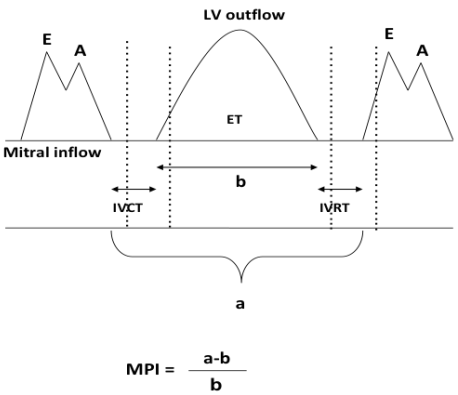

Figure 1. Schematic demonstration of the calculation of myocardial performance index. a- Time interval between the initiation and end of mitral inflow, b- Left ventricular ejection time, IVCT – isovolemic contraction time, IVRT- isovolemic relaxation time

Statistical Analysis: For the statistical evaluation of the results, SPSS for Windows Version 15.0 software was used. Data were shown as mean ± SD. Mean differences between groups were compared by Student's t test. The correlation between the variables was analyzed using Pearsons and Spearman Rank tests. Statistical significance was considered as p≤ 0.05.

RESULTS

The study enrolled 35 patients with AS and 38 controls. Clinical characteristics of the patients and controls are shown in Table I. In our study, no statistically significant difference was found between two groups, in terms of age, gender, Body Mass Index (BMI), body surface area (BSA), systolic and diastolic blood pressure (SBP-DBP), smoking, serum lipid levels and blood glucose levels. Red cell distribution width (RDW), ESR and CRP levels of AS group were found to be significantly higher compared to that of control group.

Mean disease duration of the patients was 19,14±7,51 years. Mean BASDAI was 3,81±2,57; mean BASFI was 3,69±2,79; BASMI was 9,34±2,51; ASQoL was 8,74±5,99; MASES was 1,43±2,23.

When the echocardiographic measurements were compared between two groups, no significant difference was found in terms of ARD, LVEDD, LVESD, LVEF, FS, IVSDT, LAD and E/A ratio (Table II). IVRT and IVCT were longer, ET was shorter and MPI ratio was higher in AS patients. Mean MPI values in the AS and the control group were shown in figure 2.When the indicators of diastolic dysfunction were evaluated, E/A ratio was found to be abnormal in more patients with AS than in control subjects (11 (31,4%) vs 9 (23,7%) ;p=0,466).

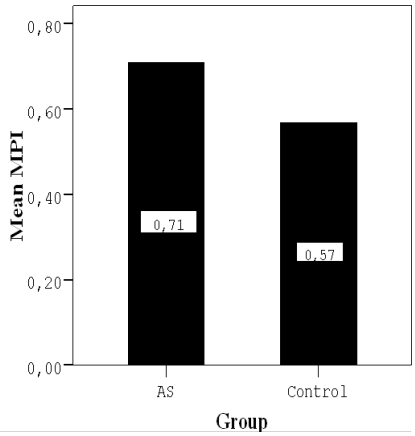

Figure 2. Mean MPI values in the ankylosing spondylitis and control groups

EF and FS, which are among the parameters of systolic function, were normal in all individuals of both groups and there was no significant difference between two groups (Table II). Correlation coefficients between MPI and several variables of the AS group were shown in Table III.

DISCUSSION

This study showed that myocardial performance index and RDW could be used for early diagnosis of the left ventricular dysfunction in patients with AS. In the studies performed in patients with AS, cardiovascular events take an important place among the causes of sudden death. It was reported that causes of cardiovascular mortality include aortic valve insufficiency , cardiomyopathy and atrioventricular block [12].

The prevelance and importance of cardiovascular diseases in rheumatologic disorders have increased due to understanding of the importance of inflammation and the immune system in cardiac disorders. Aortitis , aortic root abnormalities with aortic regurgitation , conduction system abnormalities and cardiomyopathies were the most frequent reported cardiovascular disorders in the studies including patients with AS [13,14].

Cardiac involvement appears to occur as a result of diffuse increase in myocardial connective tissue which may cause diastolic and systolic dysfunction. Although

diastolic filling abnormalities have been described in ankylosing spondylitis, LV systolic dysfunction and hypertrophy have not been reported in the absence of significant aortic regurgitation in the previous studies [15,16].

Table I: Clinical characteristics of ankylosing spondylitis and control groups

	AS Group N=35	Control Group N=38	P
Age (years)	44,69±9,03	43,13±8,59	0,453
Gender (M/W)	26/9	28/10	0,954
BMI (kg/m2)	25,80±6,49	26,18±5,27	0,785
Body surface area (m2)	1,83±0,19	1,87±0,18	0,340
Smoking status (n) (Smokers/ non-smokers)	17/18	12/26	0,626
Systolic blood pressure (mmHg)	122,14±15,59	123,55±14,79	0,693
Diastolic blood pressure (mmHg)	78,86±8,05	80,66±7,55	0,327
TChol (mg/ dL)	194,57±40,43	199,50±43,59	0,601
HDL-Chol (mg/dL)	49,06±11,48	45,76±11,01	0,215
LDL-Chol (mg/dL)	124,29±38,12	128,32±37,84	0,652
TG (mg/dL)	112,94±55,94	132,00±60,20	0,167
Glucose (mg/ dL)	89,20±14,18	89,37±16,83	0,963
ESR (mm/ hour)	24,86±17,24	13,42±9,63	0,001*
CRP (mg/dL)	0,85±0,90	0,26±0,24	<0,001*
Hemoglobin , g/L	13.71±1.75	14.42±1.57	0,061
WBC Count	8212±1945	7592±2237	0,190
Platelet Count	262975±73680	244950±70358	0,267
RDW	14,88±1,77	13,53±1,23	<0,001*
MPV	8,48±1,11	8,49±0,82	0,964
NLR	1,92±0,76	1,78±0,48	0,351
Neutrophil Count	4717,75±1639,69	4202,50±1365,78	0,131
Lymphocyte Count	2611,75±741,33	2446,75±848,61	0,357

Kuloglu et al. reported that left ventricle systolic functions were preserved where diastolic functions were impaired in patients with AS [17]. In other two studies, frequency of LV diastolic dysfunction in AS patients was found to be 20% and 26% respectively [18,19]. Moyssakis et al. analyzed the cardiac functions of 57 patients with AS and compared it with that of 78 healthy subjects. In this study patients with AS had increased aortic stiffness and decreased global myocardial performance ; and authors suggested that the abnormal Tei index may reflect an early manifestation of cardiac dysfunction in these patients [20]. Furthermore , in a study by Ustun et al ., it has been shnown that patients with AS had impaired left ventricular systolic function as assessed by speckle tracking echocardiography despite no clinical evidence of cardiovascular disease [21]. Rosa et al., published a study conducted 22 AS patients and 22 healthy individuals where patients with AS had impaired ventricular performance as measured by myocardial performance index [22]. Similiar to the previous studies , Chen et al. , evaluated left ventricular function by speckle tracking echocardiography in AS patients. They found impaired LV function and increased carotid intima media thickness in these patients [23]. Inflammatory process was thought to be the cause of ventricular dysfunction in AS. Chronic inflammatuar infiltration in myocardium , in the adventitia of the valves and cusps and fibrous proliferation in the intima was shown in previous histopathologic studies [14,24]. Systolic dysfunction in AS may occur following diastolic dysfunction as a result of diffuse myocardial infiltration and fibrosis. LV systolic dysfunction diffuse myocardial infiltration and fibrosis.

Myocardial performance index , which is an index derived from doppler measurements, appears to have a prognostic value in many clinical conditions for evaluating cardiac functions. This method combines systolic and diastolic intervals and allows to evaluate global ventricular function using a non invasive method. The fact that it is not influenced by heart rate , ventricular geometry ,blood pressure and valvular heart disease [25].

Table II: Echocardiographic data of the patients with AS and of the control group

	AS Group n=35	Control Group n=38	p
ARD (mm)	28,97±3,34	28,29±2,28	0,308
LVEDD (mm)	47,89±3,92	47,53±4,25	0,709
LVESD (mm)	30,63±3,94	30,45±3,63	0,611
EF %	66,29±6,64	65,74±4,40	0,376
FS %	36,83±5,93	36,21±3,39	0,582
IVS DT (cm)	0,93±0,13	0,89±0,08	0,128
LAD (mm)	33,11±4,55	33,76±3,54	0,497

Table III: Correlation coefficients between MPI and several variables of the AS group

	Age	BMI	ESR	CRP	SBP	DBP	LA	EF	RDW	NLR	MPV
MPI											
r	0,175	0,059	0,278	0,136	0,022	0,169	-0,099	-0,078	0,372	0,028	0,002
p	0,121	0,605	0,013	0,233	0,846	0,135	0,384	0,492	0,001	0,805	0.988

MPI : myocardial performance index, BMI : body mass index, ESR : erythrocyte sedimentation rate, CRP: C-reactive protein, SBP : systolic blood pressure , DBP : diastolic blood pressure , LA : left atrium , EF : ejection fraction , RDW : red cell distribution width , NLR :Neutrophil-to-lymphocyte ratio, MPV: mean platelet volume

E/A	1,14±0,37	1,28±0,39	0,120
ET (msn)	261,83±28,84	287,66±24,01	<0,001*
IVRT (msn)	111,77±21,04	102,02±20,58	0,049*
IVCT (msn)	70,63±15,15	58,87±22,39	0,01*
MPI	0,71±0,15	0,57±0,18	<0,001*

ARD : aortic root diameter, LVEDD: left ventricular end-diastolic diameter,LVESD: left ventricular end-systolic diameter, LVEF : ejection fraction, FS : fractional shortening,IVSDT : interventricular septum diastolic thickness, LAD: left atrium diameter ,E : Mitral E wave velocity, A: Mitral A wave velocity,ET : Ejection time,IRT :isovolemic relaxation time , ICT :isovolemic contraction time , MPI : myocardial performance index. Dat are expressed as mean ± standard deviation.

In our study , there was no statistical difference between AS group and the control group in terms of diastolic parameters. Although ejection fraction and fractional shortening was similiar in both groups, the AS group showed worse indices of left ventricular myocardial performance index in comparison with the control group. Red cell distribution width (RDW) is a measure of the size variation and an index of the heterogenity of erythocytes. It has been showed that , increased RDW represented the inflammatory status in the body [26]. Red cell distribution width (RDW) was suggested as a potential marker for predicting mortality in different patient groups and in the general population. A large number of studies have described an independent association between increased RDW and cardiovascular disease [27,28,29]. Furthermore RDW has been recently discovered as a new marker in heart failure and most of the studies have investigated RDW as a prognostic marker in patients with chronic heart failure [30,31].

In a study by Peng et al., AS patients wihout drug treatment and healthy individuals were evaluated. AS patients with increased RDW showed significant difference compared to healthy individuals along with systematic inflammatory reaction [32]. Our study revealed that RDW values were significantly higher in the patients with AS than control group in agreement with study done Peng et al. According to the data in our study , AS patients without any cardiovascular symptoms had worse indices of myocardial performance. In addition , we showed a significant positive correlation between RDW and MPI.

If the patients are asymptomatic, subclinical left ventricular dysfunction could be underdiagnosed in AS patients. Early determination of pre heart failure stage in asymptomatic patients may therefore have therapeutic and prognostic implications. Myocardial performance index may be useful for the early diagnosis of potential heart failure , by providing an earlier diagnosis of left ventricular dysfunction in patients with AS. Also RDW can be used as marker for the left ventricular function in patients with AS until an echocardiography assesment for the patients is done.

In conclusion, RDW which is routinely measured and reported as a component of the standart complete blood count , was significantly correlated with myocardial performance index for evaluation of left ventricular function in patients with ankylosing spondylitis.

Conflict of interest: The authors declare that there are no actual or potential conflicts of interest in relation to this article.
Financial Support: There is no any source of funding or financial interest in this

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How to cite this article/Bu makaleye atıf için:
Kocabas H, Kucuk M, Oncel CR, Yıldırım AB, Kacar C. Red Cell Dıstrıbutıon Wıdth and Subclınıcal Left Ventrıcular Dysfunctıon In Patıents Wıth Ankylosıng Spondylıtıs. Acta Med. Alanya 2018;2(2):96-101. DOI:10.30565/medalanya.393936