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Color and Tissue Doppler Echocardiographical Findings in Patients with Rheumatoid Arthritis

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ABSTRACT

Aim: *Cardiac involvement associated with rheumatoid arthritis (RA) is one of the common inflammatory diseases of silent nature. In this study, presence of cardiac involvement was investigated by echocardiographic evaluation in RA patients.*

Material and Methods: *Fourty-eight patients with RA and 22 age-matched healthy controls were included in this study. All individuals were evaluated in terms of clinical and laboratory parameters. Conventional and tissue Doppler echocardiography was performed.*

Results: *According to the conventional and tissue Doppler evaluation, RVD (Right ventricular diastolic diameter), RAD (Right atrium diastolic diameter), Mit-E (Early diastolic wave of mitral valve), Tleft-Em (Left ventricular lateral wall tissue Doppler late diastolic wave), Tright-Em (Right ventricular free wall tissue Doppler early diastolic wave), Mit-E/Mit-A, Tleft-Em/Tleft-Am (Left ventricular lateral wall tissue Doppler late diastolic wave/ Left ventricular lateral wall tissue Doppler late diastolic wave), Tright-Em/Tright-Am were found to be significantly lower in the RA group. Mit-A (Late diastolic motion of mitral valve), DT (Mitral deceleration time), Tleft-Am, Tright-Am (Right ventricular free wall tissue Doppler late diastolic wave), IVRT (isovolumic relaxation time), LV-MPI (Left ventricular myocardial performance index), RV-MPI (Right ventricular myocardial perfusion index) were found to be significantly higher in the RA group.*

Conclusion: *Conventional and tissue Doppler measurements demonstrated the presence of diastolic dysfunction in RA patients. Conventional and tissue Doppler electrocardiographic evaluation offers necessary, non-invasive, and practical methods in the planning of the required treatment regimen for cardiac involvement within the context of the follow-up of the RA patients.*

Keywords: diastolic dysfunction, doppler echocardiography, rheumatoid arthritis

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INTRODUCTION

Rheumatoid arthritis (RA) is a disease that requires particular attention because of the loss of function and social and psychological problems arising from the damage it does to joints and organs. It is a condition of the immune system that can cause damages to almost any organ by itself or via the adverse effects of the agents administered for its treatment. It brings about increased systematic and cardiovascular risks and accordingly shortens the life span by an average of 3 to 18 years (1). The cardiovascular disease is the most common attributed cause of death, followed by infections, pulmonary and renal disease (2). Cardiac conditions associated with RA include pericardial effusion, valvular disorders, and arrhythmias (3). RA can cause diastolic dysfunction (4), producing a unique effect on myocardial function (5). Left ventricular diastolic dysfunction (LVDD) leads to mechanical abnormalities, including decreased distensibility, impaired relaxation and abnormal diastolic filling of the left ventricle, irrespective of the ejection fraction (EF) (6). LVDD is usually attributable to common structural abnormalities such as hypertrophy, interstitial fibrosis and impaired myocyte relaxation resulting from ischaemia (7). Since LVDD is one of the prediction parameters for cardiac involvement in RA patients without overt cardiac disease, we aimed to evaluate cardiac involvement in RA by using conventional and tissue Doppler findings.

MATERIALS AND METHODS

The present study was conducted on 48 patients followed up by reason of diagnosed RA without a known heart disease at the rheumatology clinic of the faculty of medicine of a university along with 22 healthy controls. Detailed medical histories were collected from and thorough clinical examinations were performed on all individuals. Laboratory testing included the following parameters for all individuals: C-reactive protein (CRP), rheumatoid factor (RF), whole blood count (WCB), and erythrocyte sedimentation rate (ESR). Patients with RA were selected from among those observed during routine clinic visits and the members of the control group from among individuals not exhibiting disease presence. Those included in the study did not present cardiovascular findings such as palpitation, hypotension, syncope, chest pain, and dyspnoea. Written consent was collected from all individuals to indicate their voluntary participation in the study.

Exclusion criteria

Patients with a history of acute rheumatic fever or exhibiting hypertension, cardiomyopathy, congenital heart conditions, peripheral vascular impairment, coronary heart disease, heart failure, valvular heart disease, rhythm disorders, electrolyte disorders, antiarrhythmic or psychotropic drug

use, diabetes mellitus, central nervous system diseases, chronic kidney disease, liver disease, thyroid disease, malignancy pregnancy, respiratory failure or other rheumatic disorders were excluded from the study.

Disease Activity Criteria

Disease activity was identified through the use of DAS 28, a disease activity index assessing 28 joints. For the purposes of this index, the number of tender joints (NTJ) and the number of swollen joints (NSJ) were specified from amongst shoulder, elbow, wrist, metacarpophalangeal (MCP), proximal interphalangeal (PIP), first carpometacarpal, thumb interphalangeal, and knee joints on both sides, and the total number was recorded accordingly. At the same time, DAS 28 score was calculated for every patient on the basis of the respectively identified ESR. In this scoring system, scores below 2.6 are considered to point to remission; between 2.6 and 3.2 to low disease activity; between 3.2 and 5.1 to moderate disease activity; and above 5 to severe disease activity.

Echocardiographic Evaluation

All patients underwent echocardiographic evaluation in left lateral position in line with the guidelines of the American College of Cardiology/American Heart Association through the employment of the SONOS 7500 with two-dimensional and M-mode recording capability and a 2.5-3.25 MHz transducer. The echocardiography measured ejection fraction, peak early filling time, peak late filling time, and E/A ratio, mitral deceleration time, and isovolumic relaxation time (IVRT). On the other hand, the evaluation of systolic function parameters was conducted through the quantification of M-mode echocardiographic findings from the parasternal long axis, septal and posterior wall thicknesses, and cardiac end-diastolic and end-systolic widths on the basis of their associations with ECG. Valve regurgitations were evaluated through echocardiographic measurements in colour and pulsed Doppler modes. The following variables were evaluated as left ventricular filling indices: peak early (E) and peak late (A) transmittal filling velocities and their ratio (E/A), descending slope of E leg (EF slope) and deceleration time (DT), and isovolumic relaxation time (IVRT – the time between the closure of the aortic valve and the onset of transmitral flow).

All M-mode and two-dimensional echocardiographic measurements were made on the basis of at least 3 consecutive cardiac cycles.

The following global or local systolic and diastolic functions of the ventricles were evaluated through tissue Doppler imaging: those imagings were interventricular septal diastolic diameter (IVSDd), left ventricular diastolic diameter (LVDd), interventricular septal systolic diameter (IVSSd), left ventricular systolic diameter (LVDSd), left ventricular ejection fraction (EFleft), right

ventricular ejection fraction (EFright), left atrium diameter (Lad), aortic root (AR), right ventricular diastolic diameter (RVDd), right atrium diastolic diameter (RADd), early diastolic wave of mitral valve (MIT-E), late diastolic motion of mitral valve (MIT-A), early diastolic motion of mitral valve / late diastolic motion of mitral valve ratio (MIT-E/MIT-A), mitral deceleration time (MDT), isovolumic relaxation time (IVRT), tissue Doppler for early diastolic motion in left ventricular lateral wall (Tleft-Em), tissue Doppler for late diastolic motion in left ventricular lateral wall (Tleft-Am), left ventricular diastolic dysfunction (Tleft-Em/Tleft-Am), tissue Doppler for early systolic motion in left ventricular lateral wall (Tleft-Sm), aortic valve maximum flow velocity (AV), pulmonary valve maximum flow velocity (PV), tissue Doppler for early diastolic motion in right ventricular lateral wall (Tright-Em), tissue Doppler for late diastolic motion in right ventricular lateral wall (Tright-Am), right ventricular diastolic dysfunction (Tright-Em/Tright-Am), tissue Doppler for early systolic motion in right ventricular lateral wall (Tright-Sm), pulmonary arterial pressure (PAP), left ventricular myocardial performance index (LV-MPI), and right ventricular myocardial performance index (RV-MPI).

Statistical Analysis

Data collected were analyzed by using the Statistical Package for the Social Sciences (SPSS 15.0). Results were expressed as mean±standard deviation. Statistical significance was tested using Mann Whitney U test. In addition, the Chi-square was used for categorical variables. The level of statistical significance was set at a two-tailed p-value of 0.05.

RESULTS

The characteristics of the RA and control groups are demonstrated in Table 1. In this context, no significant difference was identified between the two groups.

The laboratory parameters observed in the RA and control groups are presented in Table 2. Sedimentation, CRP, RF, leukocyte and thrombocyte values were found to be significantly higher in the RA group when compared to the control group ($p< 0.05$).

The findings obtained through Doppler and tissue Doppler echocardiography are shown in Tables 3 and 4. The evaluation of such measurements indicated significantly lower values in the RA group than in the control group in terms of RVD, RAD, MIT-Em, Tleft-Em, Tright-Em, Mit-Em/Mit-Am, Tleft-Em/Tleft-Am, and Tright-Em/Tright-Am. On the other hand, Mit-Am, DT, IVRT, Tleft-Am, Tright-Am and SVMPI values were identified to be significantly higher among the RA patients than the control group.

Table 1. Characteristics of rheumatoid arthritis and control groups

	RA group (%)	**Control group (%)**	**p value**
Age (years)	52,0 ± 9,4	47,1 ± 6,1	0,308
Height (cm)	157,26	161,77	0,169
Weight (kg)	70,98	71,07	0,982
Sex, Female (n,%)	35 (72,9)	11 (50,0)	0,102
Smoking status (n,%)	10 (20,83)	2 (9,09)	0,84
Alcohol (n,%)	2 (4,17)	2 (9,09)	0,521
Duration of complaints (years)	10,46 ± 8,83		
Duration of diagnosis (years)	7,11 ± 5,97		
Duration of morning stiffness (min)	102,31 ± 103,42		

Table 2. Laboratory values of rheumatoid arthritis and control groups

	RA group	**Control group**	**p value**
Sedimentation (mm/h)	35,58 ± 25,59	8,41 ± 7,07	**0,000**
C-Reactive Protein (mg/dl)	25,76 ± 33,89	4,29± 3,46	**0,004**
Rheumatoid Factor (U/L)	250,95 ± 497,52	20,13± 0,60	**0,034**
Haemoglobin (mg/dl)	12,80 ± 1,43	13,49 ± 1,34	**0,059**
WBC (10^3/µl)	9,21 ± 2,90	7,46 ± 1,98	**0,013**
Platelet count (10^3/µl)	305,70 ± 125,93	233,14± 51,5	**0,012**

Table 3. Doppler echocardiographic findings of rheumatoid arthritis and control groups

	RA group	**Control group**	**p value**
IVSD	1,03 ± 0,17	1,04 ± 0,13	0,763
LVDD	4,50 ± 0,44	4,50 ± 0,34	0,984
IVSS	1,27 ± 0,17	1,25 ± 0,12	0,595
LVDS	3,37 ± 0,38	3,43 ± 0,39	0,501
EF-LEFT	63,21 ± 9,40	64,00 ± 2,00	0,698
EF-RIGHT	60,73±3,44	59,95 ± 4,46	0,430
LAD	3,36±0,41	3,31 ± 0,38	0,604
A.KOKU	2,66±0,37	2,71 ± 0,40	0,596
RVD	3,38±0,42	3,67±0,36	0,006
RAD	3,53±0,40	3,76±0,36	0,022
MIT-EM	0,64±0,11	0,71±0,12	0,014
MIT-AM	0,82±0,20	0,66±0,10	0,001
MIT-EM/MIT-AM	0,82±0,21	1,08±0,10	0,000
DT	250,00±31,08	180,91±25,43	0,000
IVRT	112,08±14,73	88,18±11,81	0,000

Abbreviations: *DT: Deceleration time; EFleft: Left ventricular ejection fraction; EFright: Right ventricular ejection fraction; IVRT: Isovolumic relaxation time; IVSDd: Intraventricular septal diastolic diameter; IVSSd: Intraventricular septal systolic diameter; LAd: Left atrium diameter; LVDd: Left ventricular diastolic diameter; LVDSd: Left ventricular systolic diameter; MDT: Mitral deceleration time; MIT-A: Mitral valve late diastolic wave; MIT-E: Mitral valve early diastolic wave, RADd: Right atrium diastolic diameter; RVDd: Right ventricular diastolic diameter*

DISCUSSION

In this study we aimed to evaluate the cardiac involvement in patients with RA by using conventional and tissue doppler echocardiography.

Patients with RA present an increased risk for cardiovascular diseases. Almost half of all deaths among RA patients are caused by cardiovascular conditions that are mostly observed in the form of myocardial infarction or congestive heart failure. Therefore, morbidity and mortality can be argued to mainly stem from ischemic heart disease rather than rheumatoid heart disease in these patients. But still, the underlying mechanism is yet to be fully unveiled (8). Cardiac involvement is a finding identified through post-mortem and echocardiographic analyses. The evaluation of diastolic function is performed through the utilisation of conventional Doppler, Tissue Doppler Imaging (TDI) and some other techniques. Impaired longitudinal motion in myocardial fibre is a known symptom of early myocardial dysfunction and ischemia. Consequently, TDI is a tool of importance when conducting routine echocardiography. It holds great potential for the diagnosis of diastolic left ventricular dysfunction as it is free from the disadvantages arising from conventional Doppler techniques that are affected by various factors (9).

Table 4. Tissue Doppler echocardiographic findings of rheumatoid arthritis and control groups

	RA group	Control group	p value
Tleft-EM	9,21 ± 2,16	12,39 ± 1,95	**0,000**
Tleft-AM	13,04 ± 2,62	10,55 ± 1,78	**0,000**
Tleft-SM	9,49 ± 3,75	9,62 ± 3,68	0,892
Aortic velocity	1,26 ± 0,21	1,30 ± 0,25	0,541
Pulmonary velocity	0,88 ± 09,13	0,89 ± 0,14	0,912
Tright-EM	9,02 ± 1,76	12,11 ± 1,71	**0,000**
Tright-AM	16,79 ± 0,41	11,26 ± 1,63	**0,000**
Tright-SM	13,01 ± 3,12	13,17 ± 3,01	0,837
Pulmonary arterial syst pressure	26,74 ± 7,31	26,70 ± 4,95	0,988
LV-MPI	0,55 ± 0,18	0,49 ± 0,05	0,044
RV-MPI	0,57 ± 0,21	0,22 ± 0,03	**0,000**
TleftE/TleftA	0,72 ± 0,18	1,20 ± 0,26	**0,000**
TrightEm/TrightAm	0,59 ± 0,24	1,08 ± 0,07	**0,000**

Abbreviations: *LV-MPI: Left ventricular myocardial performance index; AV: Aortic valve maximum flow velocity; PAB: Pulmonary arterial pressure; PV: Pulmonary valve maximum flow velocity; RV-MPI: Right ventricular myocardial perfusion index; Tright-Am: Right ventricular free wall tissue Doppler late diastolic wave; Tright-Em: Right ventricular free wall tissue Doppler early diastolic wave; Tright-Em/Tright-Am: Right ventricular diastolic dysfunction; Tright-Sm: Right ventricular free wall tissue Doppler systolic wave; Tleft-Am: Left ventricular lateral wall tissue Doppler late diastolic wave; Tleft-Em: Left ventricular lateral wall tissue Doppler early diastolic wave; Tleft-Em/Tleft-Am: Left ventricular diastolic dysfunction; Tleft-Sm: Left ventricular lateral wall tissue Doppler systolic wave*

LVDD in RA is attributable to usual structural changes such as ischemia-induced myocyte relaxation, interstitial fibrosis and hypertrophy (9). In addition, there are a number of mechanisms that can be held responsible for diastolic disorder, including fibrotic scarring of cardiac muscle, nodular granulomatosis, myocarditis or arthritis, amyloidosis, and cardiotoxic regimens adopted in the treatment of RA (10). Collagen accumulation and myocardial fibrosis induced by increased fibroblast activity with potential effects on both ventricles might account for the etiological mechanism. In the post-mortem studies, approximately 20% of patients are reported to exhibit myocardial fibrosis and inflammation (10).

Dyslipidaemia, atherogenic lipoprotein factors, adhesion molecules, and proinflammatory cytokines, including interleukin-1 and TNF, assume an important role in endothelial dysfunction and damage. The clinical symptoms of inflammation have been associated with mortality and morbidity in these patients (10). Inflammation, atherogenesis and thrombosis may accelerate the

development of congestive heart failure. Medical treatment against inflammation might affect the patient's risk profile for cardiovascular diseases. For instance, chloroquine has cardiotoxic side effects. Sulphasalazine, methotrexate, non-steroidal anti-inflammatory drugs, and steroids are not known to cause cardiotoxic side effects. However, it is still possible for these agents, which are frequently administered for the treatment of RA, to be among the causes of diastolic dysfunction of the heart (9).

Corticosteroids can cause hypertension, dyslipidaemia, and diabetes and lead to an increased risk for atherosclerosis. However, beneficial anti-inflammatory effects of corticosteroids are also suggested in a number of studies for patients with a history of coronary heart disease (10). Endothelial dysfunction is observed among early-stage and long-term RA patients. A previous study reported endothelial dysfunction in 32 young and middle-aged RA patients exhibiting no cardiovascular risk factors and low disease activity (8). Subclinical myocardial dysfunction, described as diastolic dysfunction, is frequently observed in RA patients and has been found to correlate with the severity of disease (11). In addition, 40-50% of all deaths in RA have been associated with cardiovascular mortality. In this context, an increased prevalence is reported among RA patients, and it is suggested to occur earlier in RA patients in comparison with the general population (12). A considerable number of RA patients exhibit signs of right ventricular diastolic dysfunction. Systolic or diastolic dysfunction is a result of cardiac involvement in these patients. Doppler echocardiography is a useful non-invasive method that can be employed for determination of systolic and/or diastolic dysfunction and cardiac anomalies of RV and LV. TDI is very instrumental in the evaluation of local or global left ventricular function through the measurement of annular and myocardial velocities. The same technique can also be employed for the evaluation of RV function through the measurement of tricuspid annulus and local myocardial velocities. Velocity measurements of RV free wall and tricuspid annulus by TDI may offer useful information on the systolic and diastolic functions of the right ventricle (12). A number of studies (13, 14, 15) examined E, A, and E/A ratio from among conventional mitral Doppler parameters for the evaluation of LV diastolic function in RA patients. Among these parameters, E and E/A ratio were found to be lower in RA patients when compared to the control group. In agreement with the literature data, Birdane et al. did not find any statistically significant differences in Em and Am velocities and Em/Am ratio, atrioventricular Doppler parameters, and pulmonary venous Doppler flows, but identified longer DT and IVRT among RA patients (10).

Sufficient knowledge is available concerning age-associated progressive diastolic dysfunction in RA patients (9). Di Franco et al. pointed to a triple correlation between duration of

disease and E/A ratio from amongst mitral flow parameters (16). Montecucco et al. argued for the presence of a correlation between diastolic dysfunction and duration of disease in RA patients (17). The tissue Doppler imaging of mitral annular motion has been used to rectify the effect of myocardial relaxation on transmitral flow and is employed as a good predictor of diastolic function (18).

The present study investigated diastolic flow waves through the use of PW Doppler on left ventricular mitral valve. The analysis of the data obtained through such investigation indicated a decrease in the MIT-Em wave velocity and an increase in MIT-Am wave velocity. As a result, the MIT-Em/MIT-Am ratio, which is considered to be an indicator of diastolic dysfunction, was observed to be <1. Furthermore, longer DT and IVRT were identified as parameters of diastolic dysfunction. These data were found to be statistically significant when compared to those in the control group. This result is of a supportive nature for those studies conducted on the same matter before. Arslan et al. established a positive correlation between the duration of disease and diastolic parameters, and our study indicated the same correlation with Tright-Em as one of the Doppler parameters (9). A review of the study results indicated the size of the right ventricle to be within the normal limits but wider in the control group than in the RA group. RV diastolic dysfunction in RA is attributable to a number of mechanisms. LV diastolic dysfunction in RA might arise from hypertrophy, interstitial fibrosis, inflammation, vasculitis or relaxation impairment induced by ischemia. Nevertheless, such structural abnormalities affect not only LV, but also the whole heart. For this reason, RV diastolic dysfunction may be observed in RA patients. Previous studies reported the most common causes of right ventricular dysfunction as LV dysfunction and a variety of its pathophysiological aetiologies (12). Ventricular interdependence through interventricular septum is a prominent mechanism for RV diastolic dysfunction.

In addition to the aforementioned, pulmonary fibrosis can also lead to right ventricular diastolic dysfunction. RA patients have been reported to develop hypertension. This is generally a result of a pulmonary pathology. The degree of the length of right ventricular IVRT has also been associated with the degree of pulmonary arterial pressure in chronic obstructive pulmonary disease (12). Similarly, Tei et al. reported longer IVCT and IVRT in primary PHT when compared to the general population (19). The present study did not find any RA patient with pulmonary hypertension.

Within the scope of the present study, we performed tissue Doppler examinations on left ventricular lateral wall and right ventricular free wall. These examinations revealed a decrease in Tleft-Em and Tright-Em wave velocities and an increase in Tleft-Am and Tright-Am wave velocities. The Tleft-Em/Tleft-Am and Tright-Em/Tright-Am ratios, which are considered to be indicators of diastolic

dysfunction, were calculated to be <1, as was the case with the conventional Doppler technique. These data were found to be statistically significant when compared to those in the control group. These results point to the presence of diastolic dysfunction identified through the use of tissue Doppler imaging in RA patients.

MPI calculation was conducted to specify an indicator of global ventricular performance. A statistically significant difference was determined between the MPI values of both ventricles in the RA group when compared to the controls as a result of separate calculations performed for right and left ventricles. This study established, in support of the data compiled by the relevant literature, that RA patients experienced a deteriorated global performance of both ventricles in addition to diastolic dysfunction.

In conclusion, Doppler and tissue Doppler imaging points to the presence of diastolic dysfunction in RA patients. Conventional and tissue Doppler electrocardiographic evaluation offers the necessary non-invasive and practical methods in the understanding of cardiovascular interaction and the planning of the required treatment regimen within the context of the follow-up of patients with RA.

Limitations of the Study

Neither the present study nor the previous studies could reach an absolute judgment on causal links because of their cross-sectional nature. In addition, the low number of patients and control group addressed by the present study or the previous studies can also be considered a limitation.

REFERENCES

1. Pincus T, Kavanaugh A, Sokka T. Benefit/risk of therapies for rheumatoid arthritis: underestimation of the "side effects" or risks of RA leads to underestimation of the benefit/risk of therapies. Clin Exp Rheumatol 2004; 22(35): 2-11.
2. Book C, Saxne T, Jacobsson LT. Prediction of mortality in rheumatoid arthritis based on disease activity markers. J Rheumatol 2005; (32): 430–4.
3. Van Doornum S, McColl G, Wicks IP. Accelerated atherosclerosis. An extraarticular feature of rheumatoid arthritis? Arthritis Rheum 2002; 46: 862-73. 4. Renjith AS, Marwaha V, Aggarwal N, Koshy V, Singal VK, Kumar KVSH. Prevalence of left ventricular dysfunction in rheumatoid arthritis. J Family Med Prim Care 2017; 6(3): 622-6.
5. Giles JT , Fernandes V , Lima JA , Bathon JM . Myocardial dysfunction in rheumatoid arthritis: epidemiology and pathogenesis. Arthritis Res Ther 2005; 7(5):195–207.

6. Fukuta H , Little WC . Diagnosis of diastolic heart failure. Curr Cardiol Rep 2007; 9(3): 224–8.
7. Abdul Muizz AM, Mohd Shahrir MS, Sazliyana S, Oteh M, Shamsul AS, Hussein H. A cross-sectional study of diastolic dysfunction in rheumatoid arthritis and its association with disease activity. Int J Rheum Dis. 2011; 14(1):18–30.
8. Ciftci O, Yilmaz S, Topcu S, Caliskan M, Gullu H, Erdogan D, et al. Impaired coronary microvascular function and increased intima- media thickness in rheumatoid arthritis. J atherosclerosis. 2008; 198 (2) : 332-7.
9. Arslan S, Bozkurt E, Sari RA, Erol MK. Diastolic function abnormalities in active rheumatoid arthritis evaluation by conventional Doppler and tissue Doppler: relation with duration of disease. Clinical Rheumatology 2006; 25 (3): 294-9.
10. Birdane A, Korkmaz C, Ata N, Cavusoglu Y, Kasifoglu T, Dogan SM et al. Tissue Doppler imaging in the evaluation of the left and right ventricular diastolic functions in rheumatoid arthritis. J compilation 2007; 24 (5): 485-93.
11. Sharma A, Kaushik R, Kaushik RM, Kakkar R. Echocardiographic evaluation of diastolicdysfunction in rheumatoid arthritis – a case–control study. Mod Rheumatol 2015; 25(4): 552-7. 12. Seyfeli E, Guler H, Akoglu S, Karazincir S, Akgul F, Saglam H. et al. Right ventricular diastolic abnormalities in rheumatoid arthritis and its relationship with left ventricular and pulmonary involvement. Tissue Doppler echocardiographic study. Int J cardiovasc imaging 2007; 22 (6): 745-54.
13. Alpaslan M, Onrat E, Evcik D Doppler echocardiographic evaluation of ventricular function in patients with rheumatoid arthritis. Clin Rheumatol 2003; 22 (2): 84– 8.
14. Levendoglu F, Temizhan A, Ugurlu H, Ozdemir A, Yazici M Ventricular function abnormalities in active rheumatoid arthritis: a Doppler echocardiographic study. Rheumatol Int 2003; 24:141–46.
15. Vizzardi E, Cavazzana I, Bazzani C, Pezzali N, Ceribelli A, Bonadei I, et al. Echocardiographic evaluation of asymptomatic patients affected by rheumatoid arthritis. J Investig Med 2012; 60(8): 1204-8.
16. Di Franco M, Paradiso M, Mammarella A, Paoletti V, Labbadia G, Coppotelli L. et al Diastolic function abnormalities in rheumatoid arthritis. Evaluation By echo Doppler transmitral flow and pulmonary venous flow: relation with duration of disease. Ann Rheum Dis 2000; 59(3): 227–9.

17. Montecucco C, Gobbi G, Perlini S, Rossi S, Grandi AM, Caporali R. et al. Impaired diastolic function inactive rheumatoid arthritis. Relationship with disease duration. Clin Exp Rheumatol 1999; 17(4): 407–12.
18. Yazıcı D, Tokay S, Aydin S, Toprak A, Inanc N, Khan SR et al. Echocardiographic evaluation of cardiac diastolic function in patients with rheumatoid arthritis: 5 years of follow-up. Clinical Rheumatology 2008; 27(5): 647-50.
19. Tei C, Dujardin KS, Hodge DO, Bailey KR, McGoon MD, Tajik AJ. et al. Doppler echocardiographic index for assessment of global right ventricular function. J Am Soc Echocardiogr 1996; 9(6): 838– 47