

Evaluation of Ventricular Diastolic Function in Patients With Fibromyalgia Syndrome

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ABSTRACT

Objectives: This study aims to compare the diastolic functions between fibromyalgia (FM) patients and control subjects by using transthoracic echocardiography.

Patients and methods: This case-control and cross-sectional study included 34 female FM patients (mean age 43.6±8.2 years; range 28 to 57 years), who were diagnosed by The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia and defined as the FM group. A control group was defined consisting of 30 healthy females (mean age 41.2±9.1 years; range 22 to 54 years). Echocardiography findings of the groups were compared.

Results: The body mass index (BMI) and mean disease duration of the FM group were 25.37±2.71 kg/m² and 12.24 months, respectively. The BMI of the control group was 25.58±1.49 kg/m². There was no significant difference between the groups in terms of age and BMI. Isovolumetric relaxation time and mitral E-wave deceleration time values were significantly higher in the FM group than in the control group (p=0.047, p=0.003, respectively).

Conclusion: Isovolumetric relaxation time and mitral valve deceleration time are significantly prolonged in FM patients compared with healthy subjects. Female patients with FM seem to be under risk of impaired relaxation and diastolic function of the left ventricle.

Keywords: Diastolic dysfunction; echocardiography; fibromyalgia syndrome; isovolumetric relaxation time; mitral E-wave deceleration time.

Fibromyalgia (FM) is a non-inflammatory rheumatic syndrome characterized with chronic widespread pain as well as joint stiffness and systemic symptoms such as fatigue, depression, cognitive dysfunctions, and sleep disturbances.^{1,2} Previous studies have established that FM is associated with cardiovascular diseases such as nondipper circadian blood pressure variability, increased carotid intima media thickness, and coronary heart disease.³⁻⁵ Although the exact physiopathology is not known, the aforementioned studies mainly focused on inappropriate sympathetic discharges due to the autonomic nervous system changes and their impacts on blood pressure and cardiac functions. On the other hand, diastolic dysfunction (DD)

refers to a collection of mechanical problems in the contraction and relaxation of the heart. DD is an echocardiographic diagnosis and not a clinical one.⁶ However, to the best of our knowledge, DD has not been studied in FM patients yet. Therefore, in this study, we aimed to compare the diastolic functions between FM patients and control subjects by using transthoracic echocardiography.

PATIENTS AND METHODS

This case-control and cross-sectional study was conducted between June 2016 and February 2017 at Muğla Sıtkı Kocman University Medical

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Faculty Research and Training Hospital and included 34 female FM patients (mean age 43.6 ± 8.2 years; range 28 to 57 years), who were diagnosed according to The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia⁷ and defined as the FM group. In addition, a control group consisting of 30 healthy females (mean age 41.2 ± 9.1 years; range 22 to 54 years) was defined. Echocardiography findings of both groups were compared. The study protocol was approved by the Muğla Sıtkı Kocman University Clinical Research Ethics Committee. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Exclusion criteria were any previous cardiac pathologies, diabetes mellitus, malignancies, renal disorders, electrolyte imbalances, any other rheumatic or endocrine diseases, chronic drug/alcohol/smoke utilization, obesity, and pregnancy. Individuals who had a history of drug utilization for any reason in the past two weeks were excluded as well.

All examinations were performed with the same echocardiographic recorder (Philips EPIQ 7 ultrasonography system, Koninklijke Philips N.V.; Best, The Netherlands) by the same examiner who was blinded. The Simpson's method was used for left ventricular (LV) ejection fraction. Mitral inflow Doppler and tissue Doppler examinations were measured to show the left ventricle. Mitral flow E and A peak velocities, mitral E-wave deceleration time (DT), and E/A ratio (ratio of early to atrial mitral inflow peak velocity) values were measured from the apical four chamber view. Isovolumetric relaxation time (IVRT) was measured during Doppler imaging of the LV outflow. Early diastolic velocity (E') was measured at basal septal/lateral (E' septal/E' lateral) aspects of mitral annulus by pulsed-wave tissue Doppler imaging. DD was defined according to recommendations for the evaluation of LV Diastolic Function by echocardiography from the American Society of Echocardiography and the European Association of Cardiovascular Imaging.⁸ Patients with normal LV systolic functions were included to the examinations. E/Em (Em= E' lateral and E' septal mean) ratio was calculated to estimate LV filling pressure, and participants with an average ≤ 8 ratio were considered with normal LV filling pressure.⁹

Statistical analysis

IBM SPSS version 20.0 (IBM Corp., Armonk NY, USA) statistical package was used for the statistical assessments. Normality of the variables was evaluated with the Shapiro-Wilk test. Statistical differences between the groups were performed with the independent samples t-test. Relationship between the variables was detected by Pearson's correlation. A *p* value of 0.05 was set as the significance level.

RESULTS

The body mass index (BMI) and mean disease duration of the FM group were 25.4 ± 2.7 kg/m² and 12.24 months, respectively. The BMI of the control group was 25.6 ± 1.5 kg/m². There was no significant difference between the groups in terms of age and BMI.

Echocardiography findings of the groups were compared in Table 1. IVRT and mitral E-wave DT values were significantly higher in the FM group than in the control group ($p=0.047$, $p=0.003$, respectively). There was no statistically significant difference between the groups according to E, A, E/A, E/E' septal, E/E' lateral and E/E mean values (all $p>0.05$).

DISCUSSION

In this study, we aimed to explore whether LV diastolic functions change in FM patients compared to control subjects by using transthoracic echocardiography. The most significant result of this study was that IVRT and mitral E-wave DT was significantly prolonged in FM patients.

Autonomic dysfunction is taken into account as a major feature of FM. Aberrant autonomic nervous system responses cause sympathetic hyperactivity and reduced parasympathetic activity.^{10,11} Besides, impaired cardiac innervation is related to ventricular dysfunction.¹² It has been shown that hyperactivation of the sympathetic fibers provide inotropic support to the failing heart and peripheral vasoconstriction to maintain arterial pressure.¹² This neurohormonal exacerbation can have deleterious responses on myocytes. They can lead to decreased neuronal

Table 1. Echocardiographic features of study groups

	FM group (n=34)	Control group (n=30)	p
	Mean±SD	Mean±SD	
Heart rate (beat/min)	74.5±11.0	70.2±10.3	0.139
Left atrium diameter (cm)	3.1±0.3	3.1±0.4	0.888
Aort diameter (cm)	2.9±0.3	2.8±0.3	0.122
Left ventricular ejection fraction	62.1±4.5	60.7±6.1	0.388
Fractional shortening	36.3±2.8	35.4±3.5	0.285
E (cm/s)	0.8±0.2	0.9±0.2	0.305
A (cm/s)	0.7±0.2	0.6±0.2	0.075
E/A ratio	1.2±0.3	1.4±0.4	0.667
E/E' lateral	6.2±2.8	6.1±2.1	0.487
E/E' septal	7.5±2.7	7.2±2.2	0.612
E/E' m	6.8±2.4	6.6±1.9	0.734
Interventricular septal thickness (cm)	0.9±0.1	0.9±0.1	0.741
Posterior wall thickness (cm)	0.9±0.1	0.9±0.1	0.752
Left ventricular end-diastolic diameter (cm)	4.2±0.4	4.2±0.3	0.928
Left ventricular end-systolic diameter (cm)	2.6±0.3	2.7±0.3	0.559
Isovolumetric relaxation time (ms)	98.6±24.2	88.5±10.6	0.047
E deceleration time (ms)	245.0±38.0	211.7±40.5	0.003

FM: Fibromyalgia; SD: Standard deviation; E: Peak early diastolic velocity; A: Peak late diastolic velocity; E/A: Ratio of peak early to peak late diastolic velocities; E/E'm: Septal and lateral E/E' means.

density and cell apoptosis, a strong indicator of adverse prognosis.¹³ Rapid filling during early diastole and active filling by atrial contraction during late diastole are the main components of diastolic physiology.¹² It has been accepted DD when the IVRT is higher than 110 ms and DT is higher than 240 ms.¹⁴ In our study, we found that IVRT (98.6±24.2 ms) and mitral E-wave DT (245.0±38.0 ms) were prolonged in FM patients compared to healthy subjects. These significant prolongations are the indicators of impaired relaxation of the left ventricle of the heart. In the literature, diastolic dysfunction has been studied in some other rheumatic diseases such as rheumatoid arthritis, scleroderma, ankylosing spondylitis, and Behçet's disease.¹⁴⁻¹⁸ These studies focused on inflammatory mechanisms, vasculitic and fibrotic changes of the heart which are the causes of distensibility, abnormal diastolic filling, impaired relaxation, and diastolic stiffness of the left ventricle. However, FM is a non-inflammatory disorder different from the aforementioned rheumatic diseases. The mechanism of the prolonged IVRT and DT in our study could be attributed to the inappropriate sympathetic discharges of the autonomic nervous system.

Cardiac afterload, particularly related to arterial stiffness, affects ventricular relaxation adversely and it was previously reported that FM patients

had significantly increased arterial stiffness compared with the healthy controls. In addition, conflicting findings as regards catecholamine and adrenergic dysregulation in FM have been previously reported. Catecholamine induced persistent activation of calcium channels may play a role in the mechanism of the impaired relaxation of myocardial/endothelial cells which can lead to arterial stiffness related distensibility of the left ventricle.^{19,20} Therefore, it can be asserted that arterial stiffness may be another possible mechanism of the impaired LV relaxation findings of the FM subjects.

Our study has some significant limitations. First, the study was conducted in a single tertiary center and the sample size was small. Second, the sample comprised only female subjects. Third, the study lacks intra- and inter-rater reliability of the echocardiographic evaluation. Last, we did not evaluate the patients according to the new classification criteria for FM patients and any test/scale for disease activity and their association with DD.

In conclusion, we may state that IVRT and mitral E-wave DT were significantly prolonged in our study population. Our results are noteworthy because female patients with FM seem to be under risk of impaired relaxation and diastolic function of the left ventricle. This condition should be kept in mind for proper and reasonable management

of this syndrome. Further studies with cohort design are required on this subject.

Declaration of conflicting interests

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REFERENCES

- Güler H, Yıldızgören MT, Üstün N, Paksoy H, Turhanoglu AD. Isokinetic assessment of the wrist muscles in females with fibromyalgia. *Arch Rheumatol* 2016;31:215-20.
- Sayılır S. The relationship between symptom severity and cognitive functions with obesity in fibromyalgia syndrome. *Turk J Osteoporos* 2016;22:129-31.
- Bölük H, Öztürk GT, Cömert D, Ersöz M. Increased carotid intima-media thickness in female patients with fibromyalgia: a preliminary study. *Arch Rheumatol* 2015;30:307-10.
- Inal S, İnal EE, Okyay GU, Öztürk GT, Öneç K, Güz G. Fibromyalgia and nondipper circadian blood pressure variability. *J Clin Rheumatol* 2014;20:422-6.
- Tsai PS, Fan YC, Huang CJ. Fibromyalgia is associated with coronary heart disease: a population-based cohort study. *Reg Anesth Pain Med* 2015;40:37-42.
- Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016;17:1321-60.
- Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990;33:160-72.
- Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Eur J Echocardiogr* 2009;10:165-93.
- Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA; Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. *J Am Soc Echocardiogr* 2002;15:167-84.
- Spinelli L, Pellegrino T, Pisani A, Giudice CA, Riccio E, Imbriaco M, et al. Relationship between left ventricular diastolic function and myocardial sympathetic denervation measured by (123)I-meta-iodobenzylguanidine imaging in Anderson-Fabry disease. *Eur J Nucl Med Mol Imaging* 2016;43:729-39.
- Grassi G, Seravalle G, Cattaneo BM, Lanfranchi A, Vailati S, Giannattasio C, et al. Sympathetic activation and loss of reflex sympathetic control in mild congestive heart failure. *Circulation* 1995;92:3206-11.
- Deswal A. Diastolic dysfunction and diastolic heart failure: mechanisms and epidemiology. *Curr Cardiol Rep* 2005;7:178-83.
- Kim SK, Kim KS, Lee YS, Park SH, Choe JY. Arterial stiffness and proinflammatory cytokines in fibromyalgia syndrome. *Clin Exp Rheumatol* 2010;28(6 Suppl 63):S71-7.
- Baris N, Okan T, Gurler O, Akdeniz B, Turker S, Ilknur T, et al. Evaluation of left ventricular diastolic dysfunction with conventional and current Doppler techniques in Behcet's disease. *Clin Rheumatol* 2006;25:873-6.
- Aslam F, Bandiali SJ, Khan NA, Alam M. Diastolic dysfunction in rheumatoid arthritis: a meta-analysis and systematic review. *Arthritis Care Res (Hoboken)* 2013;65:534-43.
- Vemulapalli S, Cohen L, Hsu V. Prevalence and risk factors for left ventricular diastolic dysfunction in a scleroderma cohort. *Scand J Rheumatol* 2017;46:281-7.
- Aslam F, Bandiali SJ, Crowson C, Alam M. Cardiac Function and Diastolic Dysfunction in Behcet's Disease: A Systematic Review and Meta-Analysis. *Int J Rheumatol* 2016;2016:9837184.
- Caliskan M, Erdogan D, Gullu H, Yilmaz S, Gursoy Y, Yildirim A, et al. Impaired coronary microvascular and left ventricular diastolic functions in patients with ankylosing spondylitis. *Atherosclerosis* 2008;196:306-12.
- Lee JH, Cho KI, Kim SM, Lee HG, Kim TI. Arterial stiffness in female patients with fibromyalgia and its relationship to chronic emotional and physical stress. *Korean Circ J* 2011;41:596-602.
- Light KC, Bragdon EE, Grewen KM, Brownley KA, Girdler SS, Maixner W. Adrenergic dysregulation and pain with and without acute beta-blockade in women with fibromyalgia and temporomandibular disorder. *J Pain* 2009;10:542-52.