Atrial Dispersion Predicts Atrial Fibrillation in Mitral Stenosis: A Five-Year Follow-Up Speckle-Tracking Echocardiography Study

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ABSTRACT

Introduction: Atrial dispersion showing increased electrical heterogeneity may be associated with the occurence of atrial fibrillation (AF). In our study, it was aimed to investigate the effects of atrial dispersion evaluated by speckle tracking echocardiography on the occurence of AF on in patients with mild to moderate rheumatic mitral stenosis.

Patients and Methods: Sixty-two patients with rheumatic mitral stenosis with sinus rhythm, asymptomatic or NYHA 1 symptoms were included in the study. The time to peak atrial strain was measured for each segment by speckle tracking echocardiography in two and four-chamber views. Atrial dispersion was calculated by taking the standard deviation of time to peak strain in 12 left atrial segments. Echocardiographic and clinical parameters of the patients were compared according to the development of AF.

Results: During follow-up (mean follow-up duration, 49.9 ± 12.9 months), 19 patients (30%) developed AF. Compared to patients who did not develop AF at follow-up, patients with AF were older (46.8 ± 10.2 vs. 35.9 ± 12, p= 0.001), while mitral valve area (MVA) (1.38 ± 0.1 vs. ± 1.49 ± 0.18 vs. p= 0.02), PALS (13.7 ± 4 vs. 18.8 ± 5.5, p= 0.001) and PACS (6 ± 2.3 vs. 8.2 ± 3.8, p= 0.002) were found to be lower. Atrial dispersion was found to be increased in patients who developed AF (63.2 ± 13.5 vs. 46.1 ± 22.3, p= 0.003). Age, atrial dispersion and PALS were determined as independent predictors of AF development in Cox regression analysis.

Conclusion: Atrial dispersion, a new parameter measured by STE, predicts the development of AF. Increased atrial dispersion may provide additional benefits in initiating prophylactic antiarrhythmic drug therapy or anticoagulants.

Key Words: Mitral valve stenosis; atrial fibrillation; 2D echocardiography

Mitral Darlığı Hastalarında Atriyal Dispersiyon Atriyal Fibrilasyon Gelişmesini Öngördürür: Beş Yıllık Noktacık Takipli Ekokardiyografi Çalışması

ÖZET

Giriş: Artmış elektriksel heterojeniteyi gösteren atriyal dispersiyon, atriyal fibrilasyon (AF) gelişimi ile ilişkili olabilir. Çalışmamızda hafif ve orta dereceli romatizmal mitral darlığı olan hastalarda noktacık takipli ekokardiyografi ile değerlendirilen atriyal dispersiyonun AF üzerindeki etkilerini araştırdık.

Hastalar ve Yöntem: Çalışmaya sinüs ritminde, asemptomatik veya NYHA 1 semptomları ve romatizmal mitral darlığı olan 62 hasta alındı. Zirve atriyal gerilime kadar geçen süre, iki ve dört odacıklı görüntülerde noktacık takipli ekokardiyografi ile her segment için ölçüldü. Atriyal dispersiyon, tüm 12 sol atriyal segmentte zirve gerilime kadar geçen zamanın standart sapması alınarak ölçüldü. Takip süresinde hastaların ekokardiyografik ve klinik parametreleri AF gelişimine göre karşılaştırıldı.

Bulgular: Takip süresi boyunca (ortalama takip süresi 49.9 ± 12.9 ay), 19 hastada (%30) AF gelişti. Takipte AF gelişmeyen hastalar ile karşılaştırıldığında, AF gelişen hastaların yaşı daha fazla iken (46.8 ± 10.2'ye karşı 35.9 ± 12, p= 0.001), mitral kapak alanı (MVA) (1.38 ± 0.1'e karşı 1.49 ± 0.18, p= 0.02), PALS (13.7 ± 4'e karşı 18.8 ± 5.5, p= 0.001) ve PACS (6 ± 2.3'e karşı 8.2 ± 3.8, p= 0.002), daha düşük saptandı. Ancak atriyal dispersiyon (63.2 ± 13.5'e karşılık 46.1 ± 22.3, p= 0.003) AF'si olan hastalarda artmış olarak saptandı. Çok değişkenli Cox regresyon analizinde yaş, atriyal dispersiyon ve PALS, takipte AF gelişimi için bağımsız öngörücü olarak tespit edildi.

Sonuç: Noktacık takipli ekokardiyografi ile değerlendirilen atriyal dispersiyon, AF gelişimi ile ilişkilidir. Atriyal dispersiyon, antiaritmik ilaç tedavisinin veya antikoagülan tedavinin erken başlatılması için ek bilgi sağlayabilir.

Anahtar Kelimeler: Mitral kapak darlığı; atriyal fibrilasyon; 2D ekokardiyografi

Cite this article as: *Candan Ö. Atrial dispersion predicts atrial fibrillation in mitral stenosis: A five-year follow-up speckle-tracking echocardiography study Koşuyolu Heart J 2023;26(1):27-33.*

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Submitted: 27.10.2022
Accepted: 25.01.2023
Available Online Date: 21.03.2023

INTRODUCTION

Rheumatic heart disease affects the mitral valves and causes mitral stenosis very frequently. Despite advances, morbidity causes such as peripheral and cerebral embolic events, pulmonary edema, and deterioration in quality of life are still high[1,2]. The frequency of atrial fibrillation (AF) in mitral stenosis has been found to be 30-50%[3]. In mitral stenosis, increased atrial pressure causes inflammation and interstitial fibrosis in the atrial wall, leading to a decrease in atrial wall elasticity. The structural remodeling process leads to electrical remodeling and causes AF[4]. Many clinical, echocardiographic and biochemical variables that cause AF in patients with mitral stenosis have been investigated[5-7]. Two-dimensional (2D) strain imaging as assessed by speckle tracking echocardiography (STE) has been developed to examine both ventricular and atrial myocardial function[8-11].

Atrial dispersion with electrical heterogeneity has been found to be associated with occurence of AF in the normal population[12-14]. In patients with reduced atrial dispersion, recurrence of AF was reduced after successful ablation[15].

In this study, it was aimed to investigate whether atrial strain and atrial dispersion used together with clinical parameters are associated with occurence of AF.

PATIENTS and METHODS

One hundred and twenty patients with mild or moderate rheumatic mitral stenosis were screened. Inclusion criteria were determined as patients with mild or moderate rheumatic mitral stenosis, asymptomatic patients and patients with EF> 65%, and 82 patients meeting the inclusion criteria were included in the study.

Exlucia criteria was described as anemia, chronic obstrictive pulmonary disease, hypertension, history of coronary artery intervention, NYHA class II-IV, modorate or severe aortic or mitral or tricuspid insufficiency. Eleven patients who did not come to the follow-up appointment and nine patients with inapropiate echocardiographic images were excluded from the study.

A 12-lead ECG was taken at each examination, and cardiac symptoms were evaluated. A rhythm Holter recording was done when the patient had symptoms suggestive of AF. AF was determined as rhythm without p waves and irregular RR intervals in 12 lead ECG[16].

Classic 2D-Echocardiography

All echocardiographic images were gathered by a Vivid 7 machine using a 3.5 MHz transducer. The acquired images were analyzed offline with the EchoPAC program. Data of classic 2D echocardiography and dopplers measurements were collected in accordance with the guidelines[17-20].

Speckle Tracking Echocardiography

Apical 2 and 4 chambers view has been used to evaluate left atrail strain. The narrowest volume of left atrial endocardium was marked manually. Additional lines were created automatically in the epicardial and middle myocardial regions with the software. Before the analysis, it was checked whether the line formed was visually appropriate for endocardial follow-up. If not appropriate, it was corrected again manually. Left atrial endocardium was divided into six segments.

Peak atrial longitudinal stretch (PALS) was defined as the strain in the left atrium reaching its largest volume while (PACS) was defined as the strain immediately after the p wave in the ECG. In total, strain analysis was performed on 744 segments, and 3.9% of the segments were not included in the study.

Time from the onset of the QRS complex to the peak strain was calculated for each left atrial wall segment. Standard deviation of the electrical delay of a total of 12 segments was calculated and defined as the atrial dispersion[14].

Our study adhered to the Helsinki Declaration, and all patients provided written informed consent. The Ethics Committee of Kartal Koşuyolu High Specialization Training and Research Hospital approved the study in İstanbul, Türkiye.

Statistical Analysis

In the analysis of continuous variables between the two groups, Student's t test or Mann-Whitney U test was used, depending on whether it showed normal distribution or not. $\chi 2$ or Fisher's exact test was used for categorical variables, and Pearson's correlation test was used for correlation analysis. Cox regression testing was used to identify predictors contributing to the development of AF. Variables that were significant in a single analysis were used to perform multivariate analysis. For statistical significance, p value was determined as <0.05 and SPSS (version 24.0) program was used.

RESULTS

Sixty-two patients with isolated mild-to-moderate mitral stenosis (40% male, mean age 39.2 ± 12.5 years) were included in the study. Clinical features and echocardiographic data of the study patients are shown in Table 1.

Atrial fibrillation was detected in 19 patients (30%) during the follow-up period (mean follow-up= 49.9 ± 12.9 months). Eight of these patients had paroxysmal and 11 had persistent AF.

Table 1. Echocardiographic and clinical characteristic of the study population

Variable	All patients n= 62	AF (+) n= 19	AF (-) n= 43	p
Age (years)	39.2 ± 12.5	46.8 ± 10.2	35.9 ± 12	0.001
Sex (male) (%)	25 (40%)	5 (26%)	20 (47%)	0.1
Body surface area (m^2)	1.69 ± 0.13	1.67 ± 0.12	1.7 ± 0.14	0.5
Systolic blood pressure (mmHg)	128.9 ± 8.1	129.3 ± 7.5	128.7 ± 8.4	0.7
Diastolic blood pressure (mmHg)	78.4 ± 5.7	79.8 ± 6.6	77.7 ± 5.3	0.1
Heart rate (bpm)	72.6 ± 9.1	75 ± 8.3	71.6 ± 9.4	0.1
LVEF (%)	63.8 ± 4.1	64.7 ± 4	63.3 ± 4.2	0.2
LA diameter (cm)	5 ± 0.5	5 ± 0.5	4.9 ± 0.5	0.7
LAVi (mL/m^2)	57.1 ± 15.5	62.1 ± 20.3	54.9 ± 12.4	0.1
E (m/s)	2.2 ± 0.5	2.2 ± 0.6	2.2 ± 0.6	0.8
A (m/s)	1.88 ± 0.47	1.7 ± 0.48	1.9 ± 0.47	0.2
PALS (%)	17.2 ± 5.6	13.7 ± 4	18.8 ± 5.5	<0.001
PACS (%)	7.5 ± 3.5	6 ± 2.3	8.2 ± 3.8	0.008
Pulmonary artery pressure	36.7 ± 5.7	37.1 ± 6.4	36.6 ± 5.5	0.7
Atrial dispersion (msn)	51.4 ± 21.4	63.2 ± 13.5	46.1 ± 22.3	0.001
MVA by planimetry (cm^2)	1.46 ± 0.18	1.38 ± 0.15	1.49 ± 0.18	0.025
MVA by PHT (cm^2)	1.47 ± 0.16	1.47 ± 0.16	1.46 ± 0.16	0.8
Maximum gradient (mmHg)	16.9 ± 4.8	17.3 ± 3.9	16.7 ± 5.1	0.6
Mean gradient (mmHg)	8.2 ± 3	8.4 ± 2.9	8.2 ± 3	0.7

LVEF: Left ventricular ejection fraction, LA: Left atrial, LAVi: Left atrial volume index, PALS: Peak atrial longitudinal strain, PACS: Peak atrial contraction strain, E: Peak early filling transmitral velocity, A: Peak late filling transmitral velocity, MVA: Mitral valve area, PHT: Pressure half time, PLN: Planimetric.

Patients who developed AF were older than those who did not (46.8 ± 10.2 vs. 35.9 ± 12, p= 0.001). MVA (PLN) (1.38 ± 0.15 vs. 1.49 ± 0.18, p= 0.025) and global PALS (%) (13.7 ± 4 vs. 18.8 ± 5.5, p≤ 0.001) and global PACS (%) (6 ± 2.3 vs. 8.2 ± 3.8, p= 0.008) were statistically significantly lower in patients who developed AF (Table 1) (Figure 1).

Atrial dispersion was found to be statistically significantly prolonged in patients with AF (63.2 ± 13.5 vs. 46.1 ± 22.3 p= 0.001) (Table 1) (Figures 2, 3). However, the relation between atrial dispersion and AF type (permanent or paroxysmal) could not be determined (60.8 ± 7.5 ms vs. 66.4 ± 19.2, p= 0.45). There was no significant difference between the two groups in terms of left atrial diameter, left atrial volume index, and pulmonary artery systolic pressure (Table 1).

No significant correlation was observed between atrial dispersion (ms) and age (years), left atrial diameter (cm), left atrial volume index (mL/m^2), PALS (%), PACS (%), MVA PHT, maximum gradient and mean gradient. Only a moderate correlation was observed between atrial dispersion and MVA measured by the planimetric method (r= -0.38, p= 0.002).

Multivariate regression analysis was used to identify predictors of the development of AF. Atrial dispersion, PALS, age, and MVA (PLN), which were significant in the univariate analysis, were included in regression analysis. Atrial dispersion (ms) (HR= 1.033, 95 CI= 1.009-1.059, p= 0.008), age (years) (HR= 1.045, 95% CI= 1.001-1.091, p= 0.047) and PALS (HR= 0.868, 95%) (CI= 0.783-0.963, p= 0.007) were identified as independent predictors for the development of AF (Table 3).

DISCUSSION

Decreased PALS and greater atrial dispersion are associated with the occurence of AF in mitral stenosis.

Pressure increase in mitral stenosis causes an increase in interstitial fibrosis and contributes to the deterioration of atrial relaxation. As a result, the reservoir functions of the left atrium are impaired. Thus, electrical remodeling including shortening of the atrial effective refractory period and increased refractory period distribution may lead to the development of AF[21,22].

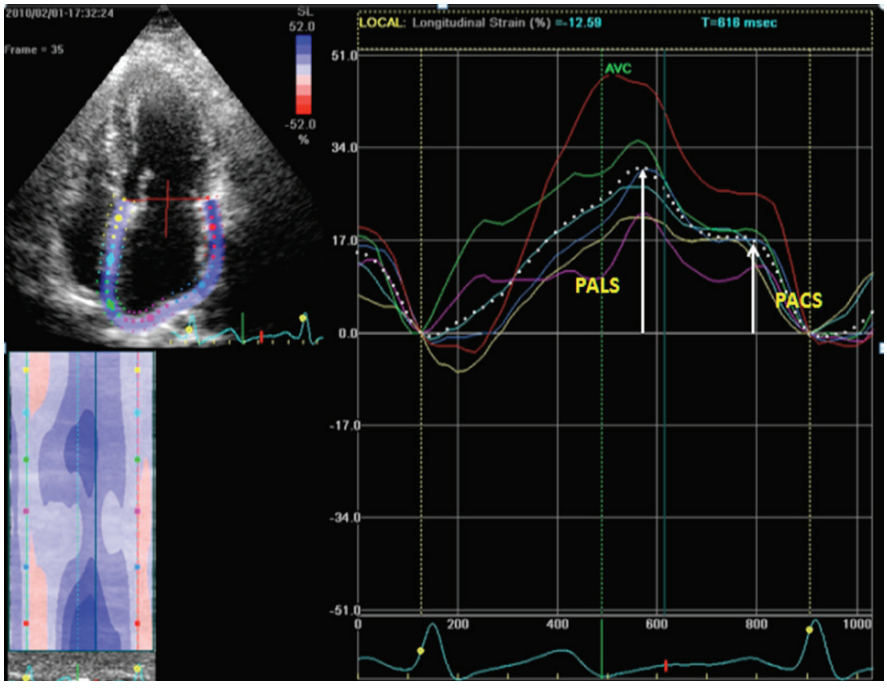

Figure 1. Left atrial longitudinal strain parameters.
PALS: Peak atrial longitudinal strain, PACS: Peak atrial contraction strain.

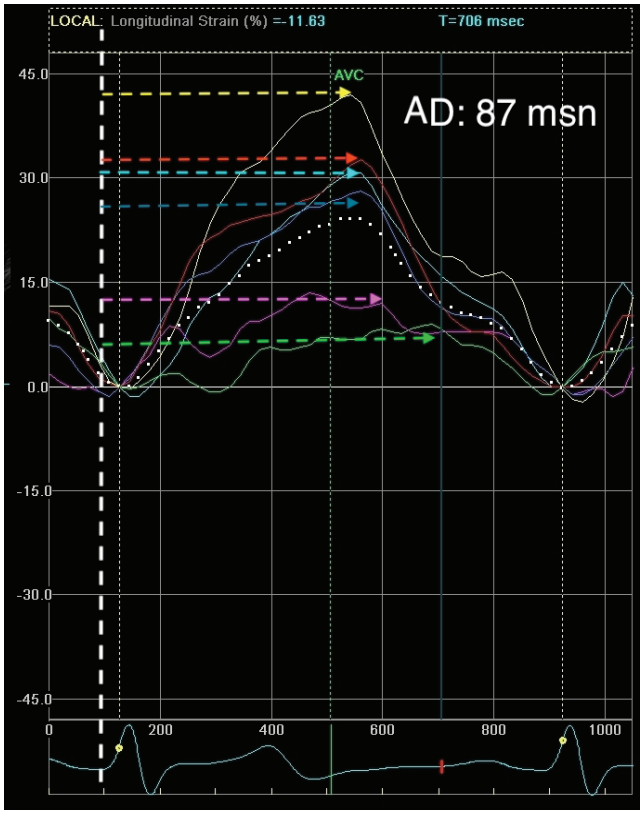

Figure 2. Speckle-based left atrial dispersion of with atrial fibrillation.
AD: Atrial dispersion.

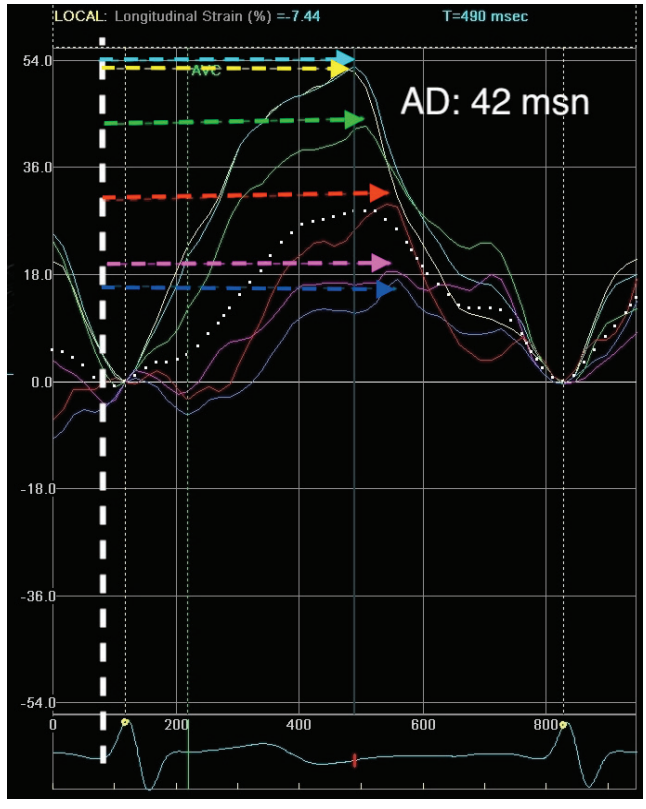

Figure 3. Speckle-based left atrial dispersion of without atrial fibrillation.
AD: Atrial dispersion.

Table 2. Correlation of atrial dispersion

Variable	r	p
Age (years)	0.52	0.6
PALS (%)	0.015	0.9
PACS (%)	0.006	0.9
LA diameter cm	-0.048	0.7
LAVi mL/m^2	-0.069	0.5
MVA (PLN)	-0.38	0.002
MVA (PHT)	0.091	0.4
Maximum gradient	0.022	0.8
Mean gradient	0.020	0.8

LA: Left atrial, LAVi: Left atrial volume index, PALS: Peak atrial longitudinal strain, PACS: Peak atrial contraction strain, MVA: Mitral valve area, PHT: Pressure half time, PLN: Planimetric.

Table 3. The results of cox regression analysis for the prediction of atrial fibrillation

Variable	B	Exp (B)	CI	p
Age (years)	0.044	1.045	1.001-1.091	0.047
PALS (%)	-0.141	0.868	0.783- 0.963	0.007
Atrial dispersion (msn)	0.033	1.033	1.009-1.059	0.008
MVA (PLN)	-1.031	0.357	0.023-5.654	0.46

PALS: Peak atrial longitudinal strain, CI: Confidence interval MVA: Mitral valve area, PLN: Planimetric.

PALS is used in the evaluation of reservoir function[9,10]. Decreased PALS may indicate impaired dilatation capacity (reservoir function) of the atrial tissue and may be useful in differentiating patients who may develop AF. PALS has been shown to be associated with the development of AF after cardiac surgery[23-25]. In addition to other echocardiographic and clinical parameters, LA strain has been found to be more accurate in predicting the development of AF in patients with mitral stenosis at follow up[26,27]. Similar to previous studies, in our study, global PALS was found to be predictive of the development of AF. Decreased PALS indicates impaired atrial reservoir function and thus, susceptibility to the development of AF.

Various diseases leading to fibrosis in the left ventricle and left atrium cause electrical asynchrony or dispersion by creating foci whose electrical stimulation occurs at different times. Subsequently, mechanical asynchrony may occur, triggering the formation of arrhythmia. Although atrial dispersion can be evaluated by various echocardiographic methods, it is more accurately and easily evaluated with speckle tracking echocardiography.

In a study of normal subjects predisposed to develop heart failure and AF, atrial dispersion has been found to be associated with the occurence of AF[28]. Atrial dispersion has been found to be associated with the occurence of recurrence in patients undergoing ablation for paroxysmal AF, and another study has found that prolonged atrial dispersion is significantly reduced after successful DC cardioversion in patients undergoing DC cardioversion in this patient group[15,29]. In a study by Kupczynska et al., increased atrial dispersion has been associated with the formation of thrombus in the atrial appendage[30]. In our study, atrial dispersion is associated with the development of AF. In patients with mitral stenosis, electrical heterogeneity in the atrial wall causes irregularities in conduction velocities and refractory periods. The resulting electrical remodeling can lead to electromechanical dysfunction and consequent development of AF[4]. According to the most recent ESC valvular diseases guideline, new onset AF contributes to the timing of decision for percutaneous mitral balloon valvuloplasty or surgical intervention in asymptomatic patients with mitral stenosis. Since atrial dispersion is also associated with AF in this patient group, it can be used to decide the time of intervention[31].

In this study, age was found to be associated with the occurence of AF. With increasing age, fibrosis in the atrial tissue increases more and leads to the development of AF[26].

CONCLUSION

Atrial dispersion as assessed by STE is associated with the development of AF. Atrial dispersion may provide additional information for the early initiation of antiarrhythmic drug therapy or anticoagulant therapy.

Limitations

The significant limitation is the study was that it was single-centered and the number of patients was relatively small. Since we did not have a special software for atrial strain assessment, the software used for ventricular strain assessment was utilized. Again, speckle tracking echocardiography evaluation was excluded from the analysis in some patients due to the requirement for good image quality. The frequency of AF may have been seen to be underestimated since the methods we used for detecting AF could not particularly detect patients with asymptomatic AF.

Ethics Committee Approval: This study was approved by Kartal Koşuyolu High Specialization Training and Research Clinical Research Ethics Committee (Decision no: 20/7/7/39, Date: 21.09.2017).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - ÖC; Analysis/Interpretation - ÖC; Data Collection - ÖC; Writing - ÖC; Critical Revision - AK; Final Approval - ÖC; Statistical Analysis - ÖC; Overall Responsibility - ÖC.

Conflict of Interest: The author have no conflicts of interest to declare.

Financial Disclosure: The author declare that this study has received no financial support.

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