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Original Article

Value of tissue Doppler imaging and peak acceleration time in prediction of paroxysmal atrial fibrillation in patients with paroxysmal atrial fibrillation

Paroksismal atriyal fibrilasyonu olan hastalarda paroksismal atriyal fibrilasyonun öngörülmesinde doku Doppler görüntüleme ve zirve hızlanma süresi

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ABSTRACT

Aim: Atrial fibrillation is the most common arrhythmia in the population and its prevalance increases with age; and also is the most morbid and mortal arrhythmia. Usually the beginning of the persistant atrial fibrillation is recurrent episodes of the paroxysmal atrial fibrillation (PAF). Prediction of the paroxysmal atrial fibrillation can cause prevention of this arrhythmia and thus prevention of the adverse outcomes. We aimed to investigate tissue Doppler imaging (TDI) and peak acceleration time (pkAcc) parameters that can predict the paroxysmal atrial fibrillation in this study.

Material and Methods: 20-73 years old (mean 47,5) 50 individuals that are diagnosed with PAF included the patient group. 50 individuals who have the similar baseline demographic charasteristics with patient group and who have no persistant or PAF included the control group. Transthoracic echocardiogaphic (TTE) evaluation is applied all of the control and study groups. Tissue Doppler parameters and pkAcc is measured in TTE and statistical analyses is performed.

Results: In TTE evaluation, left atrium ejection fraction is lower in the patient group than the study group (%50,6 vs. %59,2, p<0,001). In TDI evaluation, the average of E/E' which was measured from the anterior, inferior, lateral and septal walls of the left ventricle; is found higher in the patient group compared to the control group (8,17 vs. 7,04; p=0,004). When two groups are compared in terms of pkAcc, it was found that patient group is higher, but this difference did not reach the statistical significance (1063 vs. 994, p=0,14).

Conclusions: TDI evaluation can play an important role in prediction of paroxysmal atrial fibrillation.

Keywords: paroxysmal atrial fibrillation, transthoracic echocardiography, diagnostic imaging

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ÖZ

Amaç: Atriyal fibrilasyon, popülasyonda en sık görülen aritmidir ve prevalansı yaşla artar ayrıca en sık rastlanılan morbidite ve mortalite oluşturan aritmidir. Genellikle persistan atriyal fibrilasyonun başlangıcı paroksismal atriyal fibrilasyonun (PAF) tekrarlayan bölümleridir. Paroksismal atriyal fibrilasyonun öngörülmesi, bu aritminin önlenmesine ve dolayısıyla olumsuz sonuçların önlenmesine neden olabilir. Bu çalışmada paroksismal atriyal fibrilasyonu öngörebilecek doku Doppler görüntüleme (TDI) ve pik hızlanma süresi (pkAcc) parametrelerini araştırmayı amaçladık.

Gereç ve Yönetemler: 20-73 yaşları arasında (ortalama 47,5) PAF tanısı almış 50 kişi ile hasta grubu oluşturuldu.. Hasta grubu ile benzer temel demografik özelliklere sahip olan ve persistan veya PAF bulunmayan 50 kişi ile kontrol grubu oluşturuldu.Tüm kontrol ve çalışma gruplarına transtorasik ekokardiyografik (TTE) değerlendirme yapıldı. Doku Doppler parametreleri ve pkAcc TTE'de ölçüldü ve istatistiksel analizler yapıldı.

Bulgular: TTE değerlendirmesinde, hasta grubunda sol atriyum ejeksiyon fraksiyonu çalışma grubundan daha düşüktü (% 50,6 vs.% 59,2, p <0,001). TDI değerlendirmesinde, sol ventrikülün anterior, inferior, lateral ve septal duvarlarından ölçülen E / E 'nin ortalaması; Hasta grubunda kontrol grubuna göre daha yüksek bulundu (8,17 ve 7,04; p = 0,004). İki grup pkAcc açısından karşılaştırıldığında, hasta grubunun daha yüksek olduğu bulundu ancak bu fark istatistiksel olarak anlamlı bulunmadı (1063'e karşı 994, p = 0,14).

Sonuç: TDI değerlendirmesi paroksismal atriyal fibrilasyonun öngörülmesinde önemli bir rol oynayabilir.

Anahtar kelimeler: zirve hızlanma süresi; paroksismal atriyal fibrilasyon; doku Doppler görüntüleme

Introduction

Atrial fibrillation is the most common arrhythmia worldwide and related with increased negative outcomes such as increased cerebrovascular accident rate, heart failure and all-cause mortality [1]. Paroxysmal atrial fibrillation is defined as atrial fibrillation that can relapse from time to time and always terminate in 7 days (usually in 24 hours) spontaneously or by intervention [2,3]. Patients with paroxysmal AF have the same risk of cerebrovascular accident compared to patients with persistent or permanent AF, therefore it is important that patients with paroxysmal AF must be treated properly as patients with permanent or persistent AF [4]. Tissue Doppler imaging (TDI) is widely used today and has been studied in many cardiac pathologies [5]. MYocardial Doppler In Stress Echocardiography (MYDISE) study showed that TDI velocities are predictors of angiographic illness [6]. The ratio of "E" wave velocity, which is measured from mitral inflow by conventional PW Doppler method, to "E"' velocity measured by TDI method is strongly correlated [7]. Assessment of atrial functions by conventional echocardiography has not been thoroughly investigated and is worth investigating. Modesto et al. have shown that strain parameters may be useful in assessing atrial functions in amyloidosis [8]. In a study in which patients with non-valvular AF detected and cardioversion performed were followed for 1 year, a strong correlation was found between sinus rhythm administration and peak "A" velocity after cardioversio[9].

However, a study of tissue Doppler and peak acceleration time in the presence of paroxysmal atrial fibrillation is not available in the literature.

Materials and methods

Study Population

From June 2013 to December 2014, 50 consecutive adult patients (20-73 years old) with PAF who referred to Cardiology Clinic were enrolled. Fifty individuals who had similar demographic characteristics with patient group and who were found to have no persisting AF or PAF were included in the control group.Paroxysmal atrial fibrillation was defined as AF detected with a 12-lead ECG or rhythm holter monitorization, and with a short duration of 7 days. All patients had a 12-lead surface ECG. Patients' thyroid function tests were evaluated by routine biochemical methods. Exclusion criteria were left ventricular systolic dysfunction (LVEF <40%), presence of any valve disease, congenital heart disease, coronary artery disease, any abnormality in surface ECG during echocardiography , cardiomyopathy, permanent pacemaker, severe pulmonary disease, thyroid disease, chronic renal insufficiency (GFR <30 ml / min), acute coronary syndrome or cerebrovascular event in the last three months, use of class I or class III antiarrhythmic drugs.

Transthoracic echocardiographic evaluation:

All patients were evaluated in terms of valve structure and functions, left ventricular structure and functions, aortic and

left atrial dimensions, volume, and tissue Doppler parameters using a VIVID E9-GA000940 digital ultrasound device (Vingmed Ultrasound, GE).

TTE was performed in the left lateral decubitus position while all the patients were in sinus rhythm by connecting ECG. The left ventricular ejection fraction (EF) of the patients was separately calculated by the modified Simpson method from the apical-4 chamber and the apical-2 chamber views and analyzed by taking the mean values. Left atrial volume was measured by modified Simpson method from apical-5 chamber and apical-2 chamber views. The electromechanical synchronization of the pulmonary artery and aorta was measured from the beginning of the QRS complex on the ECG to the end of the record-time ejection time with PW-Doppler. Pulmonary artery and aorta ejection times were measured. The cardiac output (CO) value of all patients was measured using the PW-Doppler technique from the left ventricular outflow tract. Measurements related to E wave and A wave were made by PW-Doppler on mitral inflow. The peak acceleration time (pKAcc) was measured from the slope from the beginning of the mitral E wave until peak time **(Figure 1),(Figure 2).** Averages of 5 consecutive waves were taken to minimize the error probability in the measurements. PW-Doppler recordings were taken and measurements were made from pulmonary vein. Tissue Doppler recording was taken from all myocardial basal segments and relationship between paroxysmal atrial fibrillation and these data was evaluated **(Figure 3).**

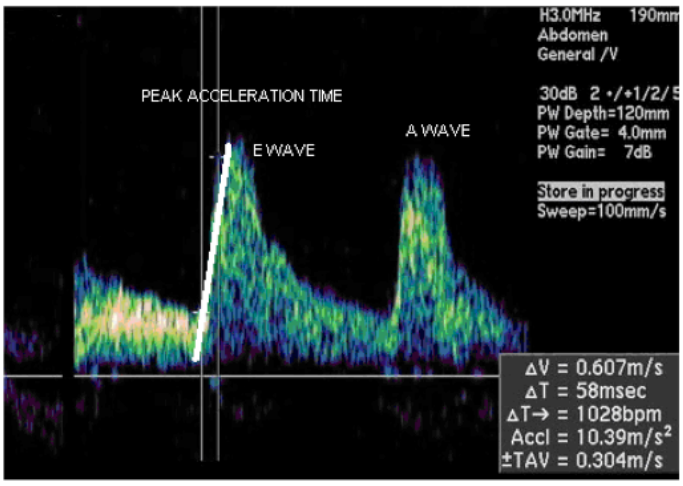

Figure-1. *Measurement of pkAcc on Mitral E wave by PW-Doppler*

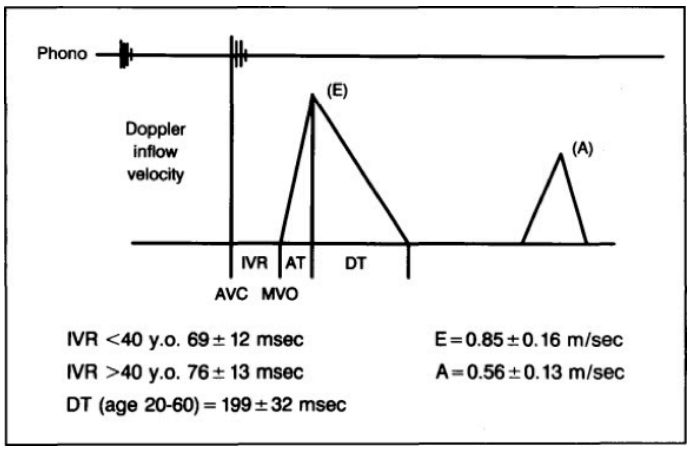

Figure-2. *Normal values of PW-Doppler mitral inflow velocities*

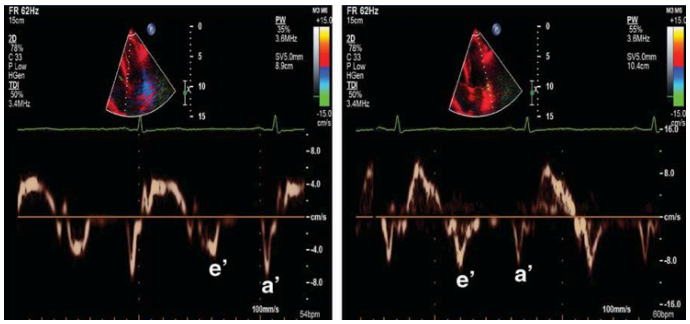

Figure-3. *Mitral septal and lateral e' and a' waves from a patient's tissue-Doppler imaging (TDI)*

Statistical analysis:

While the findings obtained in the study were evaluated, SPSS 16.0 (SPSS Inc., Chicago, Illinois) program was used for statistical analysis. Student's t-test was used for comparison between two groups of normal distribution parameters, Mann-Whitney U test was used for comparison of two groups of non-normal distribution parameters in descriptive statistical methods (mean, standard deviation, frequency) as well as quantitative data. The results were evaluated in a confidence interval of 95% and a significance level of $p < 0.05$.

Results:

Subjects on study were divided into two groups as patients with or without paroxysmal atrial fibrillation.

Demographic and clinical features:

The mean age, gender, height, weight, body mass index (BMI), HT, DM, smoking, cardiac drugs used (beta-blocker, ACE-inhibitors, ARB, CCB) were similar when baseline demographic characteristics of both groups were evaluated. There was no statistically significant difference between serum urea, creatinine, sodium, potassium, total cholesterol, triglyceride, HDL, LDL, WBC, Hemoglobin, TSH, fT3 and fT4 values in the groups **(table-1)**

Table-1. Baseline demographic characteristics of the groups

	Patient (n=50)	Control (n=50)	P value
Height (cm)	167	166	0,92
Weight (kg)	79,6	77,7	0,75
BMI	28,3	28,2	0,94
Age (years)	46,3	44,2	0,80
Female/male	23/27	27/23	0,64
Hipertension	17	14	0,42
Diabetes	9	8	0,79
Smoking	12	11	0,37
Beta-bloker	16	12	0,79
ACE-i+ARB	11	9	0,21
CCB	8	4	0,17
Urea(mg/dL)	26,5	24,9	0,08
Creatinine(mg/dL)	0,83	0,8	0,27
Sodium(mEq/L)	139,4	139,6	0,72
Potassium(mEq/L)	4,23	4,32	0,24
Total cholesterol(mg/dL)	190	187	0,70
Triglyceride(mg/dL)	163	150	0,35
HDL cholesterol(mg/dL)	38,7	41,9	0,06
LDL cholesterol(mg/dL)	118	114	0,53
WBC(x1000/uL)	8,33	8,28	0,91
Hemoglobin(g/dL)	14,0	13,5	0,06
TSH(uIU/mL)	1,81	2,09	0,11
fT3(uIU/mL)	2,68	2,67	0,88
fT4(uIU/mL)	1,41	1,49	0,22

BMI: body mass index, ACE-i: angiotensin-converting-enzyme inhibitor, ARB: angiotensin receptor blocker, CCB: calcium channel blocker, HDL: high-density lipoprotein, LDL: low density lipoprotein, WBC: White blood cell, TSH: thyroid-stimulating hormone, fT3: free triiodothyronine, fT4: free thyroxine

Echocardiographic features:

Detailed transthoracic evaluation was performed by connecting ECG to all individuals in the patient and control group. When the echocardiographic characteristics of the two groups were compared, the left ventricular end-diastolic and end-systolic diameters were similar (p=0,76). Interventricular septum and posterior wall thicknesses were significantly higher in the patient group (p=0,007 and p=0,016, respectively). Therefore, the left ventricular mass was also higher in the patient group, but this difference was not statistically significant (179.9-163.5 gr, p = 0.06). There was no difference between the groups in terms of ejection fraction and fractional shortening (65.8-65.1%, p = 0.48 and 36.3-35.8%, p = 0.48, in the patient and control groups, respectively). Left atrial end-diastolic volume was significantly higher in the patient group (41.8-36.4 mL, p = 0.003). Similarly, left atrial end-systolic volume was significantly higher in the patient group (20.3-14.5 mL, p <0.001). Ejection time measured by PW-Doppler from the left ventricular outflow tract was similar in both groups (292 ms in the patient group, 287 ms in the control group, p = 0.41). Although the stroke volume was higher in the patient group, this difference was not statistically significant (85.3-77.7 mL, p = 0.051). The mean heart rate was similar in both groups (72.9 in the patient group, 74.5 in the control group, p = 0.45). Although the cardiac output was higher in the patient group, this difference was not statistically significant (6,18-5,76 L / min; p = 0,12). In PW-Doppler recordings from the mitral inflow, the ratio of diastolic mitral "E" wave velocity to "A" wave velocity was higher in the control group (1,18-1,04; p = 0,03). When both groups were compared in terms of peak acceleration time (pKAcc), it was found that the patient group was higher but this difference did not reach statistical significance (1063-994, p = 0,14). The deceleration time (DT) of the mitral "E" wave was similar in both groups **(table-2).**

Table-2. Comparison of echocardiographic parameters in patient and control groups

	Patient group (n=50)	Control group(n=50)	P value
LVEDD (mm)	48,1	47,5	0,45
LVESD (mm)	30,6	30,4	0,76
IVS wall thickness (mm)	9,6	9,0	0,007
PW thickness (mm)	9,0	8,4	0,016
Left ventricle mass (gr)	179,9	163,5	0,06
Ejection fraction (%)	65,8	65,1	0,48
Fractional shortening (%)	36,3	35,8	0,48
Left atrial end-diastolic volume (mL)	41,8	36,4	0,003
Left atrial end-systolic volume (mL)	20,3	14,5	<0,001
Aortic diameter (cm)	2,88	2,73	0,01
LVOT diameter (cm)	2,26	2,17	0,026
LVOT ejection time (msn)	292	287	0,41
Stroke volume (mL)	85,3	77,7	0,051
Heart rate (/dk)	72,9	74,5	0,45
Cardiac output (L/dk)	6,18	5,76	0,12
E/A ratio	1,04	1,18	0,03
pkAcc	1063	994	0,14
E deceleration time (msn)	166,6	166,9	0,95

LVEDD: left ventricle end-diastolic diameter, LVESD: left ventricle end-systolic diameter, IVS: interventricular septum, PW: posterior wall, LVOT: left ventricular outflow tract, pkAcc: peak acceleration time

The ratio of the mitral "E" wave to the E' wave from the basal segment of the left ventricular anterior wall was higher in the patient group than in the control group (8,83-7,52; p = 0,014) by the tissue Doppler imaging (TDI) method. Similarly, although the E/E' ratio from the basal segment of the lateral wall was higher in the patient group, but this difference was not statistically significant (6,98- 6,50; p = 0,18). The E/E' ratio of the inferior septum basal segment was also higher in the patient group (8,68-7,77; p = 0,02). The E/E' ratio from the inferior wall basal segment was also higher in the patient group (8,17-6,36; p <0,001). There was no statistically significant difference between the two groups (5.84-5.65, p = 0.53) in the ticuspid lateral annulus E/E' ratio. When the averages of E/E' values obtained from all these segments were compared, it was found that they were significantly higher in the patient group (7,70-6,76; p = 0,007) **(table-3).**

Table 3. Comparison of TDI parameters in patient and control groups

	Patient group (n=50)	Control group (n=50)	P value
E/E' ratio (anterior)	8,83	7,52	0,014
E/E' ratio (lateral)	6,98	6,50	0,18
E/E' ratio (septal)	8,68	7,77	0,02
E/E' ratio (inferior)	8,17	6,36	<0,001
E/E' ratio (tricuspid)	5,84	5,65	0,53
E/E' ratio (left ventricle average)	8,17	7,04	0,004

In our study, left atrial end-diastolic and end-systolic volumes were significantly higher in patients with paroxysmal atrial fibrillation than in the control group (41.4 mL versus 36.4 mL, p = 0.003 and 20.3 mL versus 14.5 mL, P<0.001; respectively). Left atrial ejection fraction was also significantly lower in the patient group (50.6% versus 59.2%, p <0.001). As known, diastolic dysfunction increases left ventricular filling pressures and left atrial pressure. Also it is known that pressure increase in the left atrium plays a role in the pathogenesis of atrial fibrillation.

Although mean E/A ratio was in the normal range in both groups, it was higher in control group. This may be due to a greater number of patients with stage-1 diastolic dysfunction in the patient group than in the control group. E/E' ratio was significantly higher in the anterior wall, inferior septum, and inferior wall of the patient group, while it was not statistically significant in the lateral wall, but higher in the patient group. The mean E/E' ratio of all segments was also significantly higher in the patient group. PkAcc value was found higher in the patient group than in the control group, but this difference was not statistically significant.

Discussion

Atrial fibrillation is the most common arrhythmia and causes the most morbidity and mortality, with an increasing prevalence with age. In addition, atrial fibrillation leads to heart failure and worsens existing heart failure. In a post-hoc analysis of the AFFIRM trial, patients with atrial fibrillation and heart failure (HF-PEF: heart failure with preserved ejection fraction, SHF: systolic heart failure) were followed; and lower mortality rates were found in the HF-PEF group with high morbidity rates in both groups [10]. According to the results of this study, AF and heart failure are diseases that can cause and worsen each other. In a patient with AF, left atrial pressures increase with time, followed by increased left ventricular end-diastolic pressures, eventually resulting in left ventricular diastolic dysfunction.This results in systolic or diastolic failure in the left ventricle over time. In a patient with heart failure, left ventricular filling pressures are increased, resulting in increased left atrial pressure and ultimately the ground for AF development.

Similarly, according to CHARM trial, major cardiovascular end points in patients with atrial fibrillation was higher both in the heart failure patients with low ejection fraction and preserved ejection fraction compared to patients with sinus rythm [11]. In patients with AF, this study has shown that diastolic failure, which is often ignored, increases morbidity and mortality as well as systolic failure. Left ventricular diastolic failure is a recently developed entity, which is as morbid and mortal as systolic failure. However, it is often neglected by clinicians because of the lack of clear diagnostic criteria and the lack of effective treatment. Especially in AF patients, diastolic functions are often ignored because of limited measurement methods. In another study, the presence of atrial fibrillation in patients with heart failure with preserved ejection fraction further worsened left ventricular diastolic function; and increased hospitalization and mortality [12].

Paroxysmal atrial fibrillation should be diagnosed and treated in the same way as it is similar to persistent or permanent atrial fibrillation in terms of morbidity and mortality. Because of its importance, clinicians have done many studies to estimate it and its negative consequences. With the application of the tissue Doppler technique, the clinicians have investigated various tissue Doppler parameters in order to predict atrial fibrillation, left ventricular diastolic functions, left ventricular filling pressures and left atrial pressures. Ahmed Salah et al. [13] found that left atrial dyssynchrony measured by tissue Doppler in patients undergoing pulmonary vein isolation, was associated with subsequent atrial fibrillation recurrence. Investigators have found that patients with electromechanic dyssynchrony of 25 ms or more have a greater risk of AF recurrence and that this parameter can be measured before pulmonary vein isolation to determine which patients will benefit from the procedure.

In a retrospective study involving 840 patients over 65 years of age and greater left atrial volume, the risk of developing non-valvular atrial fibrillation was higher in patients with left ventricular diastolic dysfunction than in those without diastolic dysfunction [14]. This study is important in terms of supporting the theoretical information that left ventricular diastolic dysfunction and increased left atrial volume increase the left ventricular filling pressure, thus increase left atrial pressure and increase the risk of atrial fibrillation. However, this study was retrospective and the risk factors for atrial fibrillation such as hypertension, coronary artery disease and congestive heart failure were significantly higher in the group with atrial fibrillation. This may affect left atrial volume differences between groups. In our study, left atrial volumes were found more in the patient group and left atrial ejection fraction was found to be lower (50.6% versus 59.2%, p <0.001). In our study, coronary artery disease and congestive heart failure were excluded, hypertension was similar in both groups. We also found that there was no statistical difference in left ventricular end-diastolic diameter, end-systolic diameter, left ventricular mass, left ventricular ejection fraction, and fractional shortening between the two groups; and so a fairly homogeneous distribution of groups and difference between left atrial volumes and ejection fractions is significant. Again, only E/A ratio and mitral E deceleration-time were used to investigate diastolic functions in this study.This is why the study of echocardiographic data between 1990 and 1998 is limited and thus the parameters used to study diastolic functions are limited.In our study, tissue Doppler was used which gave very important information about diastolic functions.

In a publication in 2008, among the parameters that can be used to evaluate left ventricular diastolic function and left ventricular filling pressures in patients with atrial fibrillation; mitral "E" deceleration time, E/E' ratio, E' wave, E wave, E/Vp (ratio of mitral E wave torate of flow propagation with color M-mode), PV-DT (deceleration time of diastolic pulmonary venous flow with PW-Doppler), diastolic pulmonary venous flow velocity, pkAcc (peak acceleration time), IVRT (Isovolumic relaxation time), IVRT/T E/E' (ratio of isovolumic relaxation time to the time from the beginning of the mitral E wave to the beginning of the E' wave) are accepted [15]. Again in 2009, the same parameters were proposed in the Recommendations for the Evaluation of Left VentricularDiastolic Function by Echocardiography, jointly published by the European Society of Echocardiography and the American Society of Echocardiography [16]. In a study of left atrial ejection fraction for first atrial fibrillation or flutter detection in people over 65 years of age; the left atrial ejection fraction was found to be highly correlated withatrial fibrillation developmentindependent of left atrial volume, left ventricular function, and clinical risk factors [17]. In our study, the left atrial diastolic and systolic volumes were higher and the ejection fraction was lower in the patient group.

Raoul Stahrenberg et al. [18] performed a transthoracic echocardiography in patients with cerebral ischemia who had sinus rhythm during admission and were examined for paroxysmal atrial fibrillation with a 7-day rhythm holter. As a result, it was determined that the low ratio of left atrial volume index (ratio of left atrial volume to body surface area) to septal and lateral tissue Doppler A' wave may exclude paroxysmal atrial fibrillation. Sherif F. Nagueh et al. [19] have used Doppler echocardiography parameters to detect left ventricular filling pressure in patients with atrial fibrillation; and a formula was developed using peak acceleration time (pKAcc) and IVRT (isovolumic relaxation time).In our study, pkAcc was one of the parameters examined. Although there was a significant correlation between peak acceleration time (pKAcc) and mitral E/E', there was no significant difference between groups in terms of pKAcc.

In a study conducted in 2006, it was shown that E/E' ratio in patients with non-valvular atrial fibrillation is associated with survival and clinical outcomes [20]. In our study, there was a significant relationship between E/E' ratio and paroxysmal atrial fibrillation. If the E/E' ratio is below 8, it is consistent with normal left ventricular end-diastolic pressure; and if it is above 15, it is consistent with increased left ventricular end-diastolic pressure. Values between 8-15 are gray area and there is a wide range of diastolic function. In our study, the mean E/E' value of the patient group was 8.17; while the control group had 7.04. According to this, the left ventricular end-diastolic pressure of the control group was normal, but it remained outside the normal limits in the patient group.This demonstrates that this parameter, which shows diastolic functions, can also be used to predict paroxysmal atrial fibrillation. Although pkAcc was higher in the patient group, this difference did not reach statistical significance. This may be due to the fact that the study population is relatively small.

Limitations:

The difference in pkAcc between groups did not reach statistical significance. This can happen for a variety of reasons. One of these is that the study population is relatively small. Again, although there was a significant difference in E/E' between groups, cut-off value could not be determined by ROC analysis for E/E' values. This limits use of this parameter.

Conclusions:

The E/E' parameter used for predicting diastolic functions can also be used as a rapid, non-invasive and economical method for predicting paroxysmal atrial fibrillation in people with sinus rhythm. For this purpose, there is need for larger, randomized controlled studies in order to determine its use.

Informed consent was obtained from all the patients in the study.

Conflict of interest: Fikret Keles, Mustafa Çelik, Recep Karatas,

Ahmet Ersecgin, Ahmet Yılmaz, Nazif Aygül, Ahmet Avcı declare that they have no conflict of interest.

Figure Legends

Figure-1: Measurement of pkAcc on Mitral E wave by PW-Doppler

Figure-2: Normal values of PW-Doppler mitral inflow velocities

Figure-3: Mitral septal and lateral e' and a' waves from a patient's tissue-Doppler imaging (TDI)

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