International Journal of Pharmaceutical and Medical Research
Volume – 3 Issue – 6 December 2015
Website: www.woarjournals.org/IJPMR *ISSN: 2348-0262*

Electromechanical Abnormalities in Patients with Paroxysmal Atrial Fibrillation

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Abstract: ***Background: The loss of effective atrial contraction is associated with an increased thromboembolic risk.***

Aim: To study the electromechanical coupling of the atria in patients with paroxysmal atrial fibrillation (time of occurrence of the episodes <48 hours) using pulsed-wave tissue Doppler imaging.

Materials and methods: The study included 51 patients (26 men, 25 women; mean age 59.84±1.60 years) and 52 controls (26 men, 26 women; 59.50±1.46 years) without evidence to date for episodes of atrial fibrillation. We studied atrial electromechanical delay in lateral mitral annulus (P-A'$_{MV}$) (ms) and tricuspid annulus (P-A'$_{TV}$) (ms) as well as interatrial dyssynchrony (IAD) ((P-A'$_{MV}$) - (P-A'$_{TV}$)) (ms). The echocardiographic study in patients was performed on the twenty fourth hour and twenty-eighth day after the restoration of sinus rhythm. In controls the echocardiographic indicators were defined once.

Results: P- A'$_{MV}$ in patients with PAF was significantly prolonged compared to controls on the twenty-fourth hour as well as twenty-eighth day after the restoration of sinus rhythm (124.7±5.54 vs 106.80±2.30 ms, p=0.002; 123.2±6.12 vs 106.80±2.30 ms, p=0.006 respectively). The measurement of P- A'$_{TV}$ showed no difference in the indicator in patients and controls (91.24±4.79 vs 87.64±1.85 ms, p=0.44; 91.70±4.92 vs 87.64±1.85 ms, p=0.38 respectively). There is an increased IAD in patients with PAF compared to controls in both measurements (31.63±3.57 vs 18.64±1.35 ms, p<0.001; 31.55±2.75 vs 18.64±1.35 ms, p<0.001).

Conclusion: Our study found prolonged atrial electromechanical delay and interatrial dyssynchrony after manifestation of PAF. The short episodes of arrhythmia lead to impaired electromechanical coupling for a long period of time. In this sense AF paroxysms are a major prerequisite for relapses of the disease and significantly increase the risk of embologenic accidents.

Keywords: atrial elecromechanical delay, interatrial dyssynchrony, paroxysmal atrial fibrillation.

1. Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias in clinical practice, affecting >1% of the general population [1]. Its expression is associated with increased cardiovascular mortality and reduced physical capacity and cognitive function of patients, which determine its social significance [2].

Paroxysmal atrial fibrillation (PAF) (time of occurrence of the episodes <7 days) represents about 25% of all cases of AF, registered in outpatient and hospital settings. Normally it has a progressive clinical course and despite the ongoing anti-relapse treatment, every fourth case of the disease goes into chronic form within a few years [3, 4].

Epidemiological studies show that PAF is an important risk factor for thromboembolic accidents. The embologenic risk in PAF is 5 times higher compared to the general population and is similar to that in chronic AF [5]. It is believed that most of the cryptogenic strokes and transient ischemic attacks are a consequence of AF paroxysms [6]. They often remain asymptomatic, therefore are most likely the most undiagnosed mechanism of cryptogenic stroke. In confirmation of this fact there are a number of studies where, after prolonged Holter ECG monitoring, PAF was diagnosed in a significant percentage of patients with cryptogenic accidents [7].

It is well known that the loss of effective atrial contraction during PAF is a fundamental prerequisite for a disturbance of the laminar blood flow and the formation of coagulum. Naturally, the high embologenic potential of PAF generates significant research interest in the electromechanical function of the atria not only during arrhythmia but also in sinus rhythm. In recent years, a number of data were accumulated on the development of electromechanical disturbances in the atria in the clinical manifestation of AF. Pulsed-wave tissue Doppler imaging is a non-invasive and simple method which provides a good opportunity for their assessment [8]. It allows to study the electromechanical coupling by measuring the electromechanical delay (EMD). Atrial EMD (AEMD) by itself presents the temporal delay of the beginning of the manifest electrical activity of the atria until the initiation of atrial myocardial contraction [9, 10]. The dispersion of electromechanical coupling between the right and left atrium determines the degree of interatrial dyssynchrony (IAD). IAD alone is a risk factor for thromboembolic events.

2. Objective

To study the electromechanical coupling of the atria in patients with PAF using pulsed-wave tissue Doppler imaging.

3. Materials and Methods

3.1. Study Design

The study was conducted after the approval of the Ethics Committee of Research (№35/29.10.2010) at the University Hospital "St. Marina "- Varna and in accordance with the Declaration of Helsinki [11]. The participants were included in the study after previously signing the informed consent for participation.

In patients with PAF (time of occurrence of the episode <48 hours) echocardiographic study was conducted three times. Initially, standard echocardiography was performed, immediately after hospitalization of patients (baseline data). Subsequently, echocardiographic assessment of electromechanical coupling of the atria was performed on the twenty-fourth hour and twenty-eighth day after the restoration of sinus rhythm. In the control group echocardiography was performed once.

In the absence of contraindications specified elsewhere, restoration of sinus rhythm in patients was done with propafenone [12, 13]. Twenty-four hours after discontinuation of the rhythm disorder, the patients were dehospitalized and observed for a period of 28 days after the regularization of the rhythm. Control examinations were carried out on the seventh and twenty-eighth day after discontinuation of the PAF episodes. Careful medical history and ECG did not reveal recurrence of AF.

Propafenone was administered in the prescribed for it scheme, which lasts to a maximum of 24 hours [12, 13]. After restoration of sinus rhythm until the end of the study all patients received a maintenance p.o. propafenone dose of 150 mg three times daily.

3.2. Study participants

338 patients with PAF (time of occurrence of the episodes <48 hours), hospitalized in the Intensive Cardiology Department of First Cardiology Clinic at the University Hospital "St. Marina"- Varna for the period October, 2010 – May, 2012, were consequently screened for the study. The start of the rhythm disorder was determined by the patients as a sudden onset of a subjective feeling of "heartbeat" continuing to the time of hospitalization. The diagnosis "atrial fibrillation" was accepted after its objectification by electrocardiographic examination immediately after hospitalization of patients.

259 were excluded from the study because of presence of any of the following diseases:

1. cardiovascular diseases with the exception of mild to moderate hypertension without left ventricular hypetrophy (interventricular septum <12 mm; left ventricle posterior wall <12 mm);
2. other diseases – renal, pulmonary or hepatic failure; diseases of the central nervous system; inflammatory and/or infectious diseases in the past three months; neoplastic or autoimmune diseases; diseases of the endocrine system (with the exception of type 2 diabetes mellitus, non-insulin dependent);

or other circumstances, such as:

1. intake of hormone replacement therapy, contraceptives or analgesics, including NSAIDs;
2. pregnancy or obesity (BMI>35);
3. inability to accurately determine the onset of the arrhythmia.

23 more patients were excluded from the study because of persisting rhythm disorder after the attempt to discontinue the arrhythmia. In the remaining 56 participants (31 men, 25 women) sinus rhythm was restored with propafenone in the prescribed scheme (maximum for 24 hours) and permanently detained until the end of the study.

To balance the gender structure 51 patients were consequently selected (26 men and 25 women), mean age 59.84±1.60 years (31-77 years).

In forming the control group we applied identical exclusion criteria as in the patient group (see above). Of the 169 screened, 52 were selected as controls for the study. Their mean age was 59.50±1.46 years (30-76 years) and both men and women were an equal number – 26 (50%). Before the study the controls had no history or electrocardiographic evidence of AF.

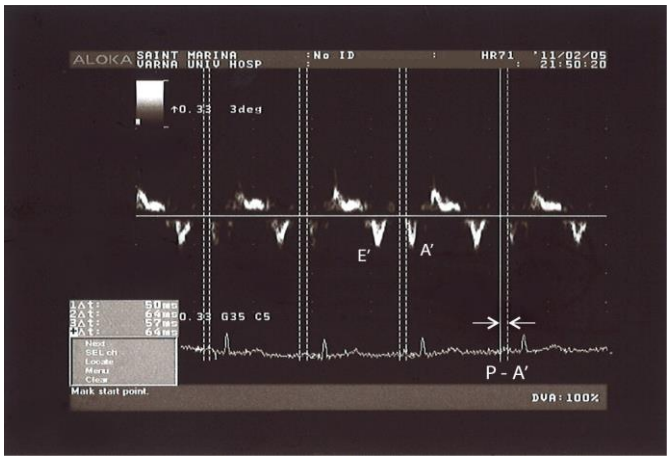
3.3. Echocardiographic methods

One-dimensional (M-mode), two-dimensional (B-mode) and Doppler echocardiography of all participants was performed in left lateral position using the apparatus Aloka ProSound SSD-4000 with 3.5 MHz probe.

In the standard echocardiography (baseline values), quantitative assessment of the internal dimensions of the left ventricle (LV) (end-diastolic and end-systolic diameter of the left ventricle), its walls (interatrial septum, posterior wall of the left ventricle) and its systolic function was done using M-mode from parasternal short axis position. The right ventricle (RV) was assessed from the apical four chamber position and its size was measured at the level of the free edge of the tricuspid valve (end diastole). End systolic (maximum) volume of the left atrium was measured from the apical four chamber position using Simpson's rule.

During sinus rhythm an assessment of atrial electromechanical coupling was done using pulsed-wave tissue Doppler imaging from the apical four chamber view. The monitor sweep speed was 100 mm/sec and the Nequisit limit was set at 15-20 sm/sec. The minimal optimal gain was used. The sample volume was placed at the level of the LV lateral mitral annulus and at the RV tricuspid annulus. The resulting tissue Doppler image is characterized with two negative (below baseline) diastolic waves - early (E ') and late (A') followed by one positive systolic myocardial wave (above baseline) [14, 15] (Figure 1).

Electromechanical delay at the level of lateral mitral and tricuspid annulus was measured as the time interval from the initiation of the P wave on the ECG until the beginning of the late diastolic TDI signal at the lateral mitral annulus (P- A'_{MV}) and the tricuspid annulus (P-A'_{TV}) (Figure 1). Interatrial dyssynchrony (IAD) was defined as prolongation of the difference between the (P- A'_{MV}) and the (P-A'_{TV}) intervals ((P-A'_{MV}) - (P-A'_{TV})). All pulsed-wave tissue Doppler indicators were measured during three consecutive heartbeats and the mean value was taken into account.



The echocardiographic methods and performed measurements were in accordance with the recommendations of the European Association of Cardiovascular Imaging at the European Society of Cardiology [16]. The echocardiographic study was synchronized with a single channel ECG.

4. Results

4.1. Subjects' characteristics

Table 1 summarizes the data from the demographic and clinical characteristics of the participants. The patient group was comparable to the controls in terms of number, mean age and sex structure (p>0.05) (Table 1). There was also no significant difference in terms of accompanying diseases, dyslipidemia and ongoing treatment (until hospitalization), as well as frequency of bad habits and BMI (p>0.05) (Table 1).

Table 1. Demographic and clinical characteristics of patients and controls.

	Patients with PAF	Control group	P values
Number of participants in the group	51	52	p=0.89
Mean age (years)	59.84±1.60	59.50±1.46	p=0.87
Men/Women	26/25	26/26	p=1/ p=0.93
Accompanying diseases			
Hypertension	37 (72.54%)	34 (65.38%)	p=0.44
Diabetes mellitus type 2	3 (5.88%)	2 (3.84%)	p=0.62
Chronic ulcer disease	2 (3.92%)	0	p=0.15
Status after hysterectomy	2 (3.92%)	1 (1.92%)	p=0.54
Benign prostatic hypertrophy	1 (1.96%)	0	p=0.32
Dyslipidemia	4 (7.84%)	3 (5.77%)	p=0.69
Medicaments for Hypertension and Dyslipidemia			
Beta blockers			
ACE inhibitors			
Sartans	19 (37.25%)	17 (32.69%)	p=0.62
Statins	15 (29.41%)	14 (26.92%)	p=0.78
	11 (21.57%)	9 (17.31%)	p=0.58
	4 (7.84%)	3 (5.77%)	p=0.69
Deleterious habits			
Smoking	8(15.69%)	7(13.46%)	p=0.75
Alcohol intake	7(13.72%)	6(11.53%)	p=0.74
BMI (kg/m^2)	23.85±0.46	24.95±0.45	p=0.09

The performed statistical analysis of the time of onset of the AF until hospitalization showed that all 51 patients were hospitalized between the second and the twenty-fourth hour after the onset of the arrhythmia, and most frequently in the fifth hour (Mo=5, 10 of all 51 patients). The mean duration of the episodes of AF until hospitalization was 8.14±0.76 hours.

4.2. Transthoracic echocardiography

The patient group did not differ from the controls in respect of basic echocardiographic indicators, namely: walls, interior size and pumping function of the left ventricle volume of the left atrium and right ventricle size (Table 2).

Table 2. Comparison of precardioversion echocardiographic measurements (baseline evaluation).

	Patients with PAF	Control group	P values
Echocardiographic indicators			
LVEDD (mm)	52.57±0.58	52.29±0.57	p=0.73
LVESD (mm)	34.43±0.56	34.73±0.48	p=0.69
EF (%)	62.98±0.70	61.54±0.58	p=0.12
IVS (mm)	10.37±0.23	9.92±0.26	p=0.20
PW (mm)	10.24±0.21	9.73±0.28	p=0.16
LA volume (ml/m²)	22.81±0.45	23.82±0.48	p=0.13
RVEDD (mm)	30.54±1.58	29.17±1.52	p=0.18

LVEDD – left ventricular end-diastolic dimeter; LVESD – left ventricular end-systolic diameter; EF – ejection fraction; IVS – interventricular septum; PW – posterior wall; LA – left atrium; RVEDD – right ventricular end-diastolic volume

P-A'$_{MV}$ in patients with PAF was significantly prolonged compared to controls on the twenty-fourth hour as well as twenty-eighth day after the restoration of sinus rhythm (p=0.002; p=0.006 respectively) (Table 3 and 4). P- A'$_{TV}$ showed no difference between patients and controls on the twenty-fourth hour and twenty-eighth day after sinus farmacoversion (p=0.44; p=0.38 respectively) (Table 3 and 4). There was increased IAD in patients with PAF compared to controls both on the twenty fourth hour and twenty-eighth day after the restoration of sinus rhythm (p<0.001) (Table 5).

Table 3. AEMD, measured in lateral mitral annulus and tricuspid annulus on the 24th hour after the restoration of sinus rhythm (comparison between patients and controls).

	Control group	Patients (24th hour)	P value
P- A'$_{MV}$ (ms)	106.80±2.30	124.7±5.54	p=0.002
P- A'$_{TV}$ (ms)	87.64±1.85	91.24±4.79	p=0.44

Table 4. AEMD, measured in lateral mitral annulus and tricuspid annulus on the 28th day after the restoration of sinus rhythm (comparison between patients and controls).

	Control group	Patients (28th day)	P value
P- A'$_{MV}$ (ms)	106.80±2.30	123.2±6.12	p=0.006
P- A'$_{TV}$ (ms)	87.64±1.85	91.70±4.92	p=0.38

Table 5. IAD on the 24th hour and the 28th day after the restoration of sinus rhythm (comparison between patients and controls).

	Control group	Patients (24^{th} hour)	P value	Patients (28^{th} day)	P value
IAD (ms)	18.64±1.35	31.63±3.57	p<0.001	31.55±2.75	p<0.001

5. Discussion

Our study finds electromechanical abnormalities in the atria of patients who experience an episode of PAF. AEMD, measured in mitral annulus is significantly prolonged twenty-four hours after the restoration of sinus rhythm (p=0.002). The changes are not momentary and persist until the twenty-eighth day after discontinuation of the arrhythmia (p=0.006) (Table 4). Like mitral AEMD, interatrial coupling is also impaired. There is interatrial dyssynchrony on the twenty-fourth hour (p<0.001) as well as on the twenty-eighth day after the restoration of sinus rhythm (p<0.001). It is appropriate to note that the patient and control groups do not differ in a number of demographic and clinical indicators (Table 1) for which there are data that they influence atrial electromechanical coupling. The creation of such uniform groups eliminates the potential impact of these indicators and gives fair opportunity to seek closer interrelationships between AF and electromechanical changes.

It is known that interatrial conductivity plays a significant role in initiating and retaining AF. Moreover, its prolongation is proportional to the frequency of AF episodes [17, 18]. In this sense, our results have important practical significance. They show that short episodes of AF lead to impaired electromechanical coupling for a long period of time. This in turn makes them an important prerequisite for the recurrence of the disease.

Moreover, the results allow to assume with a high probability that embologenic PAF potential is not only determined by the frequency and duration of the episodes of the rhythm disorder. Post-AF episodes also present risk for the occurrence of thromboembolic events, since registration of P-wave on the ECG is not equivalent to the recovery of an organized atrial contraction. This fact gives grounds to believe that the rapid and lasting interruption of the rhythm disorder would reduce AF burden during sinus rhythm. At the same time the question arises on the need for anticoagulant treatment in cases of isolated AF.

Increased AEMDs in patients with PAF were also established in other studies. Thus, e.g. Deniz et al. measured prolonged intra-left atrial mechanical delay [19]. Similar to them, Calik et al. showed association between AEMD and the manifestation of the disease [20]. Sakabe et al. [21] also establish increased IAD in PAF. Diseases such as sarcoidosis and systemic lupus erythematosus, which are associated with an increased risk of AF, also show prolonged AEMD [22, 23].

It is well known that atrial conduction delay and electrical inhomogeneity are an important prerequisite for the manifestation of AF. Therefore we sought an opportunity to predict the clinical manifestation of the rhythm disorder through changes in the electromechanical indicators. The results show that increased amounts of AEMD are predictive of AF paroxysms [20, 24, 25].

Analyzing data from studies concerning atrial electromechanical coupling in AF, it is noteworthy that the volume of the left atrium was significantly greater than that in controls. It is well known that the structural changes in the myocardium lead to electrical inhomogeneity. In this case, precisely the remodeling of the left atrium is the most probable cause for the established electromechanical disorders. This puts into question the appropriateness of the comparison between the two groups. Unlike previously mentioned studies, the presented by us echocardiographic results showed no differences between the patient and control group. It turns out that AEMDs can be prolonged also in normal sizes of the left atrium.

6. Conclusion

Our study found prolonged atrial electromechanical delay and interatrial dyssynchrony after the manifestation of PAF. The short episodes of arrhythmia lead to impaired electromechanical coupling for a long period of time. In this sense AF paroxysms are a major prerequisite for relapses of the disease and significantly increase the risk of embologenic accidents.

References

[1] Potpara TS, Lip GY. Lone atrial fibrillation: what is known and what is to come. Int J Clin Pract. 2011;65(4):446-57.

[2] Lip G, Caterina R, Savelieva I et al. ESC Committee for Practice Guidelines 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. Eur Heart J. 2012; 33:2719–47.

[3] Camm J, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S et al. Guidelines for the management of atrial fibrillation. The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology. European Heart Journal. 2010;31: 2369–429.

[4] Kirchhof P, Auricchio A, Bax J, Crijns H, Camm J, et al. Outcome parameters for trials in atrial fibrillation: executive summary. Eur Heart J. 2007;28(22):2803-17.

[5] Hohnloser SH, Pajitnev D, Pogue J, Healey JS, Pfeffer MA, Yusuf S, Connolly SJ; ACTIVE W Investigators. Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy: an ACTIVE W Substudy. J Am Coll Cardiol. 2007;50(22):2156-61.

[6] Rabinstein AA, Fugate JE, Mandrekar J, Burns JD, Seet RC, Dupont SA, Kauffman TJ, Asirvatham SJ, Friedman PA. Paroxysmal atrial fibrillation in cryptogenic stroke: a case-control study. J Stroke Cerebrovasc Dis. 2013;22(8):1405-11.

[7] Dangayach NS, Kane K, Moonis M. Paroxysmal atrial fibrillation in cryptogenic stroke. Ther Clin Risk Manag. 2011; 7: 33–37.

[8] Rein AJ, O'Donnell CP, Colan SD, Marx GR. Tissue velocity Doppler assessment of atrial and ventricular electromechanical coupling and atrioventricular time intervals in normal subjects. Am J Cardiol. 2003;92(11):1347-50.

[9] Ermiş N, Açıkgöz N, Yaşar E, Taşolar H, Yağmur J, Cansel M, et al. Evaluation of atrial conduction time by

P wave dispersion and tissue Doppler echocardiography in prehypertensive patients. Turk Kardiyol Dern Ars. 2010;38:525-30.
[10] Özer N, Yavuz B, Can I, Atalar E, Aksöyek S, Övünç K, et al. Doppler tissue evaluation of intraatrial and interatrial electromechanical delay and comparison with P-wave dispersion in patients with mitral stenosis. J Am Soc Echocardiogr. 2005; 18: 945-8.
[11] World Medical Association Declaration of Helsinki (2008). Ethical principles for medical research involving human subjects. 59th WMA General Assembly. Seoul.
[12] Bellandi F, Cantini F, Pedone T, et al. Effectiveness of Intravenous Propafenone for Conversion of Recent-Onset Atrial Fibrillation: A Placebo-Controlled Study. Clin Cardiol. 1995;18:631-4.
[13] Bianconi L, Mennuni M. Comparison Between Propafenone and Digoxin Administered Intravenously to Patients With Acute Atrial Fibrillation. Am J Cardiol. 1998;82:584-8.
[14] Hesse B, Schuele SU, Thamilasaran M, Thomas J, Rodriguez L. A rapid method to quantify left atrial contractile function: doppler tissue imaging of the mitral annulus during atrial systole. Eur J Echocardiogr. 2004;5(1):86–92.
[15] Inaba Y, Yuda S, Kobayashi N, et al. Strain rate imaging for noninvasive functional quantification of the left atrium: comparative studies in controls and patients with atrial fibrillation. JASE. 2005;18(7):729–36.
[16] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise J, Solomon S, Spencer KT, John Sutton MS, Stewart W. Chamber quantification. J Am Soc Echocardiogr. 2005 Dec;18(12):1440-63.
[17] Cosio FG, Palacios J, Vidal JM, Cocina EG, Gomez-Sanchez MA, Tamargo L. Electrophysiologic studies in atrial fibrillation. Slow conduction of premature impulses: A possible manifestation of the background for reentry. Am J Cardiol. 1983;51:122–30.
[18] Shimizu A, Fukatani M, Tanigawa M, Mori M, Hashiba K. Intra-atrial conduction delay and fragmented atrial activity in patients with paroxysmal atrial fibrillation. Jpn Circ J. 1989;53:1023–30.
[19] Deniz A, Yavuz B, Aytemir K, Hayran M, Kose S, Okutucu S, Tokgozoglu L, Kabakci G, Oto A. Intra-left atrial mechanical delay detected by tissue Doppler echocardiography can be a useful marker for paroxysmal atrial fibrillation. Echocardiography. 2009;26(7):779-84.
[20] Calık AN, Ozcan KS, Cağdaş M, Güngör B, Karaca G, Gürkan U, Yılmaz H, Bolca O. Electromechanical delay detected by tissue Doppler echocardiography is associated with the frequency of attacks in patients with lone atrial fibrillation. Cardiol J. 2014;21(2):138-43.
[21] Sakabe K, Fukuda N, Fukuda Y, Morishita S, Shinohara H, Tamura Y. Interatrial dyssynchrony on tissue Doppler imaging predicts progression to chronic atrial fibrillation in patients with non-valvular paroxysmal atrial fibrillation. Heart. 2009;95(12):988-93.
[22] Dogdu O, Yarlioglues M, Kaya MG, et al. Assessment of atrial conduction time in patients with systemic lupus erythematosus. J Invest Med. 2011;59:281–286.
[23] Buyukoglan H, Kaya MG, Ardic I, et al. Assessment of atrial conduction time in patients with sarcoidosis. J Invest Med. 2011;59:15–21.
[24] Cui QQ, Zhang W, Wang H, Sun X, Wang R, Yang HY, Meng XQ, Zhang Y, Wang H. Assessment of atrial electromechanical coupling and influential factors in nonrheumatic paroxysmal atrial fibrillation. Clin Cardiol. 2008;31(2):74-8.
[25] Ari H, Ari S, Akkaya M, Aydin C, Emlek N, Sarigül OY, Çetinkaya S, Bozat T, Şentürk M, Karaağaç K, Melek M, Yilmaz M. Predictive value of atrial electromechanical delay for atrial fibrillation recurrence. Cardiol J. 2013;20(6):639-47.