JOURNAL OF HUMAN RHYTHM

RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ

Investigation Of The Relationship Between P Wave Dispersion And Atrial Septal Aneurysm In Pregnancy

Gebelikte P Dalga Dispersiyonu ve Atrial Septal Anevrizma Arasındaki İlişkinin İncelenmesi

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Geliş Tarihi / Received: 24.04.2019 Kabul Tarihi / Accepted: 9.08.2019

ABSTRACT

Background: Aim of this study is to determine the impact of atrial septal aneurysm on atrial electrophysiology in pregnancy by the investigation of P-wave duration and P-wave dispersion on electrocardiography.

Method: This study includes 98 pregnant women, divided in two groups according to presence of atrial septal aneurysm (ASA) (n=48 ASA positive group, n=50 ASA negative group). P-wave dispersion was calculated by using the 12-lead electrocardiogram with a speed of 50 mm/sec for each participant. Cardiac functions and morphology of the aneurysm were measured using conventional echocardiography. ASA was defined if the excursion of the septum primum into the left/right atriums exceeded 10 mm or the total excursion distance was more than 15 mm.

Results: Demographic and clinical findings were similar between ASA positive group and ASA negative group, there was no significant difference. Compared to the ASA negative group, pregnant women with ASA showed significantly longer maximum P wave dispersion (PWD) (54.10±12.42 ms vs. 37,42±14,27 ms , p = 0.0001). Similarly, the maximum duration of the P wave (Pmax) in the

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ASA positive group was significantly longer than the ASA negative group (118,35±11,41 ms vs. 110,54±9,452 ms , p=0,0004). P wave dispersion and Pmax were not correlated with age, gravida, parity, gestational week, body mass index or M mode Echocardiographic parameters.

Discussion: In this study, it was shown that P-wave dispersion is prolonged in pregnant women with atrial septal aneurysm. PWD may be a pre-determinative for atrial structural anomalies or atrial arrhythmias in pregnancy and this non invasive method should be used to predict cardiac risk at the beginning of pregnancy.

Key Words: Pregnancy, atrial septal aneurysm, P wave dispersion

ÖZET

Amaç: Bu çalışmanın amacı elektrokardiyografide P-dalga süresi ve P-dalga dispersiyonunu inceleyerek; atriyal septal anevrizmanın gebelikte atriyal elektrofizyoloji üzerindeki etkisini, saptamaktır.

Yöntem: Çalışma;Atrial septal anevrizma (ASA) varlığına göre 2 gruba ayrılan 98 gebe içermektedir.(n=48 ASA pozitif grup, n=50 ASA negatif grup). P-dalgası dispersiyonu, her katılımcı için 50 mm/sn hızında 12 elektrotlu elektrokardiyogram kullanılarak hesaplandı. Kardiyak fonksiyonlar ve anevrizmanın morfolojisi, geleneksel ekokardiyografi kullanılarak ölçüldü. ASA, septum primumun sol/sağ atriyumların içine 10 mm'nin üzerinde yer değiştirmesi veya toplam yer değiştirme hareketinin 15 mm'den fazla olması olarak tanımlandı.

Bulgular: Demografik ve klinik bulgular ASA pozitif grup ile ASA negatif grup arasında benzerdi, anlamlı fark yoktu. ASA negatif gruba kıyasla, ASA'lı gebelerde anlamlı olarak daha uzun P dalga dispersiyonu görüldü. (54.10±12.42 ms vs. 37,42±14,27 ms , p = 0.0001). Benzer şekilde, ASA pozitif grubundaki P dalgasının (Pmax) maksimum süresi ASA negatif grubundan anlamlı olarak daha uzundu.(118,35±11,41 ms vs. 110,54±9,452 ms , p=0,0004). P wave dispersion and

Pmax; yaş, gravida, parite, gebelik haftası, vücut kitle indeksi veya M modu Ekokardiyografik parametrelerle korele değildi.

Sonuç: Bu çalışmada, atriyal septal anevrizması olan gebelerde P dalgası dispersiyonunun uzadığı gösterilmiştir.PDD, gebelikte atriyal yapısal anomaliler veya atriyal aritmiler için bir ön belirleyici olabilir ve bu non-invaziv yöntem, gebeliğin başlangıcında kardiyak riskini tahmin etmek için kullanılmalıdır.

Anahtar Kelimeler: Gebelik, atrial septal anevrizma, P dalga dispersiyonu

INTRODUCTION: An atrial septal aneurysm (ASA) is a localized or generalized deformity of the interatrial septum (IAS). Generally it occurs at the level of fossa ovalis but rarely it may involve entire atrial septum which bulges into the right or left atrium or both.[1] Prevalence of ASA varies in literature but Transtorasic Echocardiography (TTE) studies estimated the rates between 0.08% and 1.2%.[2] In a large autopsy series, the prevalence of ASA was reported as 1%.[3] ASA is often associated with other atrial septal abnormalities, particularly with atrial

septal defect type ostium secundum or patent foramen ovale.[4] Association between ASA and atrial tachyarrhythmias has been suggested in previous studies.[5] Despite of its clinical importance, there were no clear guidelines about management and follow up of ASA among pregnant women. Although ASA is mainly congenital, clinical symptoms of ASA such as dyspnoea, palpitation, angina or thromboembolic accidents appear during the second or third decades of patients' lives.[6] However, pregnancy is associated with a marked plasma volume expansion and cardiac output increase, which significantly loads the cardiovascular system. The physiologic adaptations of pregnant females to these hemodynamic loading include increasing both heart rate and stroke volume and fall in vascular resistance and blood pressure.[7] Because of dyspnoea, palpitation and limitation in effort capacity are common complaints of pregnant women, diagnosis of ASA is disingenuous with pregnancy as its clinical picture is similar to a wide range of normal pregnancy complaints. Otherwise, routine cardiac screening is not recommended for all pregnant women, so it is difficult to reveal presence of ASA among pregnant women according to suspect of clinical symptoms.

Electrocardiography (ECG) is an important tool to evaluate cardiovascular complications during pregnancy. P-wave dispersion (PWD), which is the difference between the smallest and the largest P-wave lengths,. is an accurate and sensitive marker to evaluate atrial electrophysiology on ECG and a non-invasive indicator of atrial arrhythmogenicity.[8] An increase in PWD is assumed to be associated with heterogeneity in atrial conduction and therefore increases the occurrence and recurrence risk of atrial arrhythmia.[9] Since it is easy to apply, cheap and accessible, It may be a good tool to evaluate the risk of atrial arrhythmia in patients with atrial septal aneurysm among pregnant women. As a contribution to the development of new strategies about management and follow up of ASA during pregnancy, in this study it was aimed to show the impact of ASA on atrial electrophysiology in pregnancy with the evaluation of P wave dispersion on ECG and thus to anticipate clinical risks of ASA during pregnancy.

MATERIAL AND METHOD: This was a single center study conducted over a period of six months from March 2017 to September 2017 by the department of Cardiology at a tertiary deliver center, Ankara, Turkey. First trimester pregnant women of aged 17 to 42 years, referred to Cardiology Department were included in the study. Written and verbal consents were obtained from all patients. The study protocol was approved by local institutional ethics

committee (Ethics Committee number:46). All patients' medical history, demographic features (age, gravida, parity, gestational week, Body Mass Index (BMI)) and heart rate were recorded at the first admission. Patients with a history of chronic systemic disease, cardiovascular disease and/or a family history of early onset cardiovascular disease, anemia, multiple pregnancies were excluded from the study. Cases with high-risk pregnancy were additionally excluded from the study. ECG and TTE were performed for all included pregnant.

After the evaluation according to the exclusion criteria, 48 pregnant with ASA remained for further analysis . Fifty- age- matched individuals who had normal echocardiographic findings were randomly selected from the same echocardiography database as the control group. A total of 98 pregnant women who met inclusion criteria were enrolled to the study. They were divided into 2 groups according to presence of ASA. (n=48 ASA positive group , n=50 ASA negative group).

Following 10 minutes of rest, each participant underwent a surface- resting 12-lead ECG in the supine position, conducted at a speed of 50 mm/sec with an amplitude of 1 mV/cm (Montara Instrument EU 250 Electrocardiograph, Milwaukee, WI, USA). The ECG recordings were scanned with a high-resolution scanner (Scanjet 8200 flatbed scanner, Hewlett Packard, Houston, Texas, USA). All ECG recordings were transferred to a computer and ECG recordings was undertaken using digital calipers by EP Callipers, version 2.12 (EP Studios Inc. 2015-2019). The starting point of the first positive wave moving in an upward direction or the first negative wave moving in a downward direction that could be observed from the isoelectric line was considered the origin of the P-wave. The turning point of the wave toward the isoelectric line was considered the end of the P-wave. P wave dispersion (PWD) was calculated with the measured values of the longest (Pmax) and shortest (Pmin) P-waves in any lead of the 12-lead ECG (PWD = Pmax – Pmin).[11] Moreover, to minimize the measurement errors, analyses of ECG parameters (Pmin, Pmax and PWD) were performed in duplicate on two separate days.

Echocardiographic examination of the patients in both groups was performed in the left lateral decubit position using a TTE (Vivid S5 System, GE Health-care, USA). All measurements were performed by the same cardiologist. Parasternal long-axis, short-axis, and apical 4-chamber and 2-chamber images were obtained and evaluated using M-mode, 2-D, continuous wave Doppler, pulse wave Doppler, and tissue Doppler methods according to American

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Echocardiography Society criteria. The existence of aneurysmatic excursion of the interatrial septum and the presence of other associated cardiac lesions were evaluated. As reported by Agmon et al,[9] ASA was defined if the excursion of the septum primum into the left/right atriums exceeded 10 mm or the total excursion distance was more than 15 mm. Left ventricular ejection fraction was provided using Teichholtz in M-mode echocardiography. The pulsed Doppler sampling volume was placed between the tips of the mitral valve leaflets to obtain maximum filling velocities. Early diastolic flow (E), atrial contraction signal (A) and E deceleration time (DT) were measured. Isovolumetric relaxation time (IVRT) was determined as the interval between the end of the aortic outflow and the start of the mitral inflow signal.

Statistical analysis was carried out with JMP®, Version 12.0. (SAS Institute Inc., Cary, NC, 1989-2019). All the values are expressed as mean ±standard deviation. Shapiro-Wilk W test was performed to test normality of of data. Differences between independent groups were assessed by t-tests for normally distributed data and Wilcoxon Rank Sum test was used for non-normal distributions. Using Pearson correlation analysis, the relationship between P wave variables and clinical and echocardiographic variables were assessed. P-values less than 0.05 were considered significant for all statistical tests.

RESULTS: The demographic features of study population are shown in Table 1. There were no statistically significant differences between the ASA positive group and controls with respect to age, gravida, parity, gestational week, weight, height, heart rate, BMI. However; LVEDD, RAEDD, RVEDD were higher in ASA positive group compared to ASA negative group but they were in normal range for both group (p=0,029, p=0,0008, p= 0,0018) (Table 2) All participants were in sinus rhythm. Compared to the ASA negative group, pregnant with ASA showed significantly longer maximum P wave duration (PWD) (54,10 ±12.42ms vs. 37,42 ±14,27 ms, p = 0,0001). Similarly, the maximum duration of the P wave (Pmax) in the ASA positive group was significantly longer compared with ASA negative group (118,35±11,41ms vs 110,54±9,452 ms , p=0,0004).

In correlation analysis; it was seen that P wave dispersion and Pmax were not correlated with age, gravida , parity, gestational week, BMI or M mode echocardiographic parameters.

Table 1: Comparison of P wave variables for ASA positive group versus ASA negative group

Parameter	ASA NEGATIVE (n=50)	ASA POSITIVE (n=48)	P value
	Mean ± Std Dev	Mean ± Std Dev	
Age, years	26,47 ± 6,40	26,83 ± 5,75	NS
G, n	2,04 ± 1,12	2,34 ± 1,38	NS
P, n	0,76 ± 0,90	0,98 ± 1,00	NS
Gestational Age, weeks	7,66 ± 1,51	7,02 ± 1,44	NS
BMI, kg/m2	23,93 ± 4,62	24,66 ± 3,16	NS
LVEF, %	67,55 ± 2,01	67,72 ± 2,06	NS
E, m/s	0,98 ± 0,12	1,01 ± 0,14	NS
A, m/s	0,75 ± 0,10	0,78 ± 0,11	NS
IVRZ, ms	78,40 ± 13,45	75,19 ± 17,35	NS
LVEDD, cm	4,21 ± 0,35	4,38 ± 0,26	<0,05
RAEDD, cm	2,86 ± 0,30	3,06 ± 0,38	<0,001
RVEDD, cm	2,03 ± 0,24	2,18 ± 0,19	<0,01
LAEDD, cm	2,78 ± 0,38	2,90 ± 0,36	NS
HR, bpm	77,50 ± 7,33	76,94 ± 12,97	NS

NS Not significant (p>0.05); G Gravida, P parity , , BMI Body mass index, LVEF left ventricul ejection fraction, LAEDD Left atrium end diastolic diamater , LVEDD Left ventricular end-diastolic diamater, LVEF Left ventricular ejection fraction, RVEDDD Right ventricular end-diastolic diamater, ,HR Heart rate, RAEDDD Right atrial end diastolic diamater, IVRT: Isovolumetric relaxation time. E Early diastolic flow, A Atrial contraction signal.

Table 2: Clinical and echocardiographic features of atrial septal aneurysm patients and controls

Parameter	ASA NEGATIVE (n=50)	ASA POSITIVE (n=48)	P value
	Mean ± Std Dev	Mean ± Std Dev	
Pmax, ms	110,54 ± 9,45	118,35 ± 11,41	<0,001
Pmin, ms	73,12 ± 10,99	64,25 ± 7,01	<0,0001
PWD, ms	37,42 ± 14,27	54,1 ± 12,42	<0,0001

Pmax: Maximum P wave duration, Pmin: Minimum P wave duration, PWD: P wave dispersion.

DISCUSSION: Physiological changes in pregnancy such as increase in maternal intravascular and extravascular fluid volumes, atrial and ventricular size, adrenergic responsiveness and elevation in hormonal levels (Estrogen and progesterone levels) affects the mechanism of arrhythmogenesis.[10] These changes alter the electrophysiologic properties of the myocardium, thus promote arrhythmogenesis.[11] Common complaints of pregnant women such as dyspnoea, palpitation and limitation in effort capacity are also result of these physiological changes. Signs and symptoms of pregnancy can mimic heart diseases so that it may be difficult to suspect a cardiovascular disease in pregnancy and it poses a particular problem especially in pregnant women, in whom the diagnosis is often delayed or missed. Therefore, observation of the clinical predictors for maternal CVD risk at the beginning of pregnancy gains importance. The California Pregnancy-Associated Maternal Morbidity and Mortality Committee Cardiovascular Disease in Pregnancy and Postpartum Task Force suggest an algorithm that includes an overview of clinical assessment and management strategies based on risk factors, presentation signs and symptoms, vital sign abnormalities, and physical examination findings.[12] To diagnose CVD, cardiac screening to pregnant women with high clinical risk factors was advised in this Task Force. Routine cardiac screening during pregnancy is not recommended in the guidelines, however early diagnosis of cardiovascular disease is important for decreasing maternal morbidity and mortality. In this study, we aimed to analyse the effect of ASA on ECG by using PWD , thus we investigated

whether PWD as a non invasive and cheap method could be a pre-determinative for atrial structural anomalies or atrial arrhythmia in pregnancy. P-wave dispersion is a non-invasive technique providing a risk estimation for atrial arrhythmia. Although there are many studies on the relationship between ASA and cardiac arrhythmia in adult patients, to the best of our knowledge, the present study is the first in pregnant women with ASA.

ASA increases the risk of maternal morbidities as atrial arrhythmias, systemic embolism and myocardial dysfunction up to heart failure.[6] The prevalence of supraventricular arrhythmia has been reported to be 40%, atrial fibrillation (18%), atrial flutter (4%), atrioventricular nodal re-entrant tachycardia (8%), and miscellaneous (18%) in adult patients with atrial ASA.[13] There are some studies in the literature about the proarrhythmia mechanism of ASA. Russo at all, showed that the echocardiographic atrial electromechanic delay (AEMD) indices (intra-left and inter-AEMD) was significantly increased in healthy ASA subjects.[14] The heterogeneity of atrial geometry caused by ASA may lead to changes in electrophysiological dynamics of the atrial myocardium. Morelli, claimed that re-entry mechanism could be dependent on an electro anatomical barrier and/or different electrophysiological properties between ASA and the remaining atrial septum.[15] Despite of the clinical importance of ASA, in the literature there were no clear guidelines about management of such condition during pregnancy. Diagnosis of ASA may be missed in pregnancy as its clinical picture is similar to a wide range of normal pregnancy complaints. Therefore, it is important to determine predictive parameters in terms of cardiac disorder at the begining of pregnancy. Some parameters obtained from surface electrocardiography (ECG) recordings are used for determining patients at risk for the development of atrial arrhythmias. Among these parameters, PWD is the most frequently used parameter in clinical cardiology. PWD is an electrocardiographic marker associated with a nonhomogeneous and discontinuous distribution of the sinus impulse.[8] In addition, PWD is accepted as a marker of prolonged interatrial and intraatrial conduction times and atrial arhytmias.[9] In previous studies, Association between ASA and atrial tachyarrhythmias has been suggested.[5] Janion and Kurzawski showed that P-wave dispersion was higher in interatrial septal aneurysm patients than in the control subjects and it is believed that this may be related to the more frequent occurrence of atrial arrhythmia in these patients.[16]

In the present study; we have demonstrated that PWD, which is a non-invasive technique providing an estimation for the risk of atrial arrhythmia, was significantly longer in pregnant

women with ASA than the control subjects. PWD may be a predictor of structural atrial anomaly or atrial arrhythmia so we suggest that more attention should be paid to the evaluation of electrocardiographic findings in all pregnant women and PWD should be utilized as a non invasive method to identify pregnant women with structural heart disease and at risk of atrial arrhythmia. At least, pregnant women with prolonged PWD should be taken under detailed cardiac examination even if they don't have any other clinical risk factor or cardiac symptom. This finding would contribute to the improvement of the follow up strategy during pregnancy.

CONCLUSIONS: Consistent with other studies demonstrating the relationship between arrhythmia and ASA, this study indicated that the PWD and max P-wave duration were prolonged in pregnant women with ASA. As a result of our study, PWD which is a non-invasive, cheap, accessible and simple technique may be a pre-determinative for atrial structural anomalies or atrial arrytmias in pregnancy and this non invasive method should be used to predict pregnant women with cardiac risk at the beginning of pregnancy.

Declaration of Interest: The author declares no conflicts of interest.

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