RESEARCH ARTICLE / *Araştırma Makalesi*

Relationship Between Fragmented QRS Complex and Maternal Demographic Features and Echocardiographic Parameters in Pregnancy

Gebelikte Fragmente QRS Kompleksi ile Maternal Demografik Özellikler ve Ekokardiyografik Parametreler Arasındaki İlişki

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Abstract

Objective	The aim of this study was to investigate the relationship between the presence of fragmented QRS (f-QRS) complex on electrocardiography (ECG) and maternal demographic characteristics and left ventricular systolic and diastolic dysfunction on echocardiography.
Materials and Methods	473 pregnant women enrolled in this study and divided into two groups. (f-QRS positive group n=77, f-QRS negative group n=396). Maternal demographic features and echocardiographic parameters of all participants were recorded and compared between two groups.
Results	The mean age of the study population was 27.70 ± 5.62 and mean gestational week was 7.37 ± 1.55. Parity in f-QRS positive group was higher than in control group (p=0.01). There was a statistically significant trend between fragmentation frequency and parity number (p=0.002). There were no significant differences between two groups in terms of age, gestational week, heart rate, body mass index. Left ventricle end-systolic and diastolic diameters and left ventricular ejection fraction were similar between the two groups
Conclusion	The presence of f-QRS was correlated with increase in number of parity and we suggest that multiparity may be a risk factor for cardiac events during pregnancy. Pregnant women with f-QRS on their rest ECG need extra attention in terms of cardiovascular disease. By demonstrating clinical significance of f-QRS, this simple tool might be used to determine women who could be at risk for developing cardiac dysfunction in pregnancy.
Keywords	QRS fragmentation; pregnancy; echocardiography

Öz

Amaç	*Bu çalışmanın amacı, elektrokardiyografide (EKG) fragmente QRS (f-QRS) kompleksi varlığı ile maternal demografik özellikler ve ekokardiyografide sol ventrikül sistolik ve diyastolik disfonksiyonları arasında ilişkiyi araştırmaktır*
Gereç ve Yöntemler	*Çalışmaya 473 gebe dahil edildi ve iki gruba ayrıldı(f-QRS pozitif grup n=77, f-QRS negative grup n=396). Tüm katılımcıların maternal demografik özellikleri ve ekokardiyografik parametreleri kaydedildi ve iki grup arasında karşılaştırıldı.*
Bulgular	*Çalışma popülasyonunun yaş ortalaması 27.70 ± 5.62, gebelik haftası ortalama 7.37 ± 1.55 idi. f-QRS pozitif gruptaki parite kontrol grubundan daha yüksekti (p = 0.01). Fragmentasyon sıklığı ve parite sayısı arasında istatistiksel olarak anlamlı bir eğilim vardı. (p=0.002). İki grup arasında yaş, gebelik haftası, kalp hızı, vücut kitle indeksi açısından anlamlı fark yoktu. Sol ventrikül end sistolik ve diyastolik çaplar ve sol ventrikül ejeksiyon fraksiyonu iki grup arasında benzerdi*
Sonuç	*F-QRS varlığı parite sayısındaki artışla korele idi ve multiparitenin gebelikte kardiyak olaylar için bir risk faktörü olabileceğini düşünüyoruz. İstirahatinde f-QRS olan gebelerin EKG'si kardiyovasküler hastalıklar açısından ekstra dikkat gerektirmektedir. f-QRS'nin klinik önemini göstererek, bu basit araç gebelikte kardiyak disfonksiyon gelişimi riski taşıyan kadınları belirlemek için kullanılabilir.*
Anahtar Kelimeler	*QRS fragmentasyonu; gebelik; ekokardiyografi*

INTRODUCTION

Fragmented QRS complex (f-QRS) on electrocardiogram (ECG) was first detected in patients with coronary artery disease. The f-QRS is an easily evaluated non-invasive electrocardiographic parameter and has been suggested as a marker of myocardial fibrosis and scar tissues associated with arrhythmic events and worse prognosis in patients with hearts diseases.[1] Heterogeneous activity caused by myocardial fibrosis and scar tissue in the ventricles may be a possible cause of fragmentation in patients with heart disease. On the other hand, this ECG sign can be found in healthy persons too and underlying mechanisms and clinical implications of f-QRS among healthy people remain unknown. Pregnancy is a physiological clinical condition with some changes in the cardiovascular system such as a 50% increase in plasma volume, a 17% increase in heart rate, and a 50% increase in cardiac output.[2,3] The incidence and severity of arrhythmias increase during pregnancy. Although the exact mechanism is unclear, increased plasma volume, increased sympathetic activity and hormonal changes were suspected.[4] Because of dyspnoea, palpitation and limitation in effort capacity are common complaints among pregnant women; diagnosis of cardiac diseases is disingenuous during pregnancy. Since cardiovascular disease (CVD) is the most common cause of death during pregnancy and findings can be masked with normal pregnancy complaints, early diagnosis of CVD may be difficult.[5] Therefore, it is important to evaluate the findings predicting cardiac risk at the beginning of pregnancy and to reveal the relationship between these findings and maternal characteristics. For this purpose, we evaluated f-QRS as a non-invasive, easily and cheap method and a predictive marker for arrhytmogenesis and cardiac events. It would be interesting that the marker, which can be easily evaluated with surface ECG, can identify pregnant women with high cardiac risk at the beginning of pregnancy. In previous studies, some of ECG parameters have been evaluated.[6] To the our knowledge this is the first study investigates the relationship f-QRS and maternal demographic and echocardiographic parameters.

Materıal And Methods

This cross-sectional study was conducted between December 2018 and March 2019 in a tertiary delivery center, Ankara, Turkey. 473 pregnant women who admitted cardiology outpatient clinic enrolled in this study and divided into two groups (f-QRS positive group n=77, f-QRS negative group n=396). A written and verbal consent was obtained from all patients. The study protocol was approved with ethical committee number 41/2019. All patients' medical history and demographic features (age, gravida, parity, weight, height, body mass index, systolic and diastolic blood pressure) were recorded. Patients with a history of chronic systemic disease, prior cardiovascular disease (CVD), multiple pregnancies and cases with high-risk pregnancy were excluded from the study. A 12-lead ECG (AT-102, Schiller AG, Switzerland) was recorded for each pregnant at rest while in the supine position. Additionally, patients who observed any arrhythmia, pre-excitation syndrome, complete/incomplete right or left bundle branch block, left posterior or anterior fascicular block, intraventricular conduction delay (QRS duration >120 ms) or significant repolarization abnormalities and long- or short-QT syndrome on the routine 12-lead ECG were excluded from the study. Fragmentation of QRS is defined as presence of an additional R wave (R') or notching in the nadir of the S wave, or the presence of > 1 R' in at least two contiguous leads, corresponding to a major coronary artery territory on the resting 12-lead ECG.[7] Recordings were acquired at a paper speed of 25 mm/s, with 1 mV/cm standardization. Transthorasic Echocardiography (TTE) (Vivid S5 System, GE Health-care, USA) was performed and following data were recorded; left ventricle end-diastolic diameter (LVEDD), left ventricle end-systolic diameter (LVESD), left ventricular ejection fraction (LVEF%), right atrium diameter (RAEDD), right ventricle end diastolic diameter (RVEDD), left atrium end diastolic diameter (LAEDD), mitral E wave velocity (cm/s), mitral A wave velocity (cm/s), tricuspid annular plane systolic excursion (TAPSE), isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT), TAPSE. Left ventricular dimen-

sions were determined using two-dimensional directed M-Mode echocardiography in the long axis of parasternal view. Systolic function was assessed by the left ventricular ejection fraction according to the Teicholz formula. Left ventricular diastolic function was evaluated by transmitral Doppler using the pulsed-Doppler technique with 2D guidance in the apical four-chamber view. All echocardiography recordings were analyzed using standard techniques.[8]

All analyses were conducted using SAS JMP v11 (SAS Institute Inc., Cary, NC, 1989-2019). Numeric variables were given as mean ± standard deviation (SD). Normality of distributions was evaluated with Shapiro-Wilk W Test. Parameter comparison was performed with Student's t-test form normally distributed parameters and Mann-Whitney U test were used for non-normal distributions.

Results

The mean age of study population was 27.70 ± 5.62 and mean gestational week was 7.37 ± 1.55. The demographical features and echocardiographic findings of study population were listed in table 1 and table 2.

Table1. The demographical features of study population

Characteristic	f-QRS(-) (n=396)	f-QRS(+) (n=77)	p Value
Age, years	27,54 ± 5,61	28,53 ± 5,65	0,18
Parity, n	0,87 ± 0,95	1,25 ± 1,14	0,01
Weight, kg	65,44 ± 12,59	68,25 ± 13,18	0,07
Height, cm	161,04 ± 6,60	161,28 ± 6,37	0,86
BMI, kg/m2	25,24 ± 4,71	26,29 ± 5,18	0,14
Gestational week	7,34 ± 1,47	7,56 ± 1,92	0,57
HR, bmp	79,27 ± 10,80	77,62 ± 11,39	0,20

Values are presented as mean ± SD. * Mann-Whitney U test
Abbreviations: Body mass index (BMI), Heart rate (HR), QRS fragmentation negative (f-QRS (-)), QRS fragmentation positive (f-QRS (+))

Table2. The echocardiographic parameters in study population

Characteristic	f-QRS(-) (n=396)	f-QRS(+) (n=77)	p value
LVEF, %	67,63 ± 2,31	67,99 ± 2,31	0,32
E, m/s	0,99 ± 0,14	0,95 ± 0,12	0,03
E', cm/s	13,34 ± 2,06	13,07 ± 2,00	0,35
E/E'	7,56 ± 1,55	7,44 ± 1,47	0,55
A, m/s	0,77 ± 0,13	0,73 ± 0,12	0,03
A', cm/s	9,68 ± 2,31	10,29 ± 2,61	0,22
DT, msn	189,20 ± 47,22	208,38 ± 49,69	<0,01
IVRZ, ms	76,98 ± 15,74	80,38 ± 11,13	0,05
LVESD, cm	2,83 ± 0,32	2,92 ± 0,32	0,11
LVEDD, cm	4,33 ± 0,29	4,34 ± 0,28	0,65
RAEDD, cm	2,95 ± 0,33	2,97 ± 0,36	0,92
RVEDD, cm	2,12 ± 0,22	2,12 ± 0,21	0,91
LAEDD, cm	2,87 ± 0,34	2,84 ± 0,31	0,48
TAPSE, cm	2,21 ± 0,27	2,19 ± 0,16	0,53

Values are presented as mean ± SD. * Mann-Whitney U test
Left Ventricular Ejection Fraction (LVEF), Mitral E wave velocity (E), Mitral A wave velocity (A), Deceleration Time (DT), Isovolumic Relaxation Time (IVRT), Left Ventricle End-diastolic Diameter (LVEDD), Left Ventricle End-Systolic Diameter (LVESD), Right Atrium End-diastolic Diameter (RAEDD), Right Ventricle End-diastolic Diameter (RVEDD), Left Atrium End-diastolic Diameter (LAEDD), Tricuspid Annular Plane Systolic Excursion (TAPSE), Early diastolic mitral annular velocity (E'), Late diastolic mitral annular velocity (A'), QRS fragmentation negative (f-QRS (-)), QRS fragmentation positive (f-QRS (+))

There were no significant differences between two groups in terms of age, gestational week, heart rate, Body mass index. Left ventricle end-systolic and diastolic diameters and LVEF were similar between the two groups. Parity number in f-QRS positive group was higher than in control group (p=0.01). The prevalence of fragmentation increases with increasing number of parity (Figure 1).

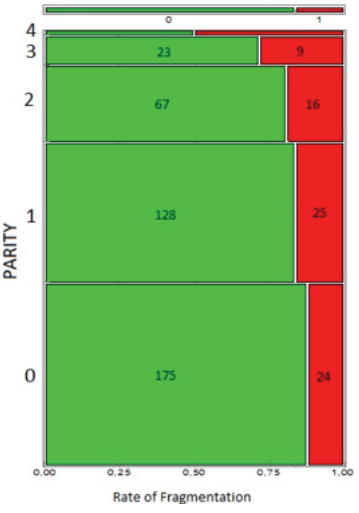

Figure 1. Mosaic Plot of the fragmentation rates by parities

Values in table 3 shows that there is a statistically significant trend between fragmentation frequency and parity number (p=0.002).

Table3. Change of Fragmentation frequency with number of parity

Parity	N (%)		p value
	f-QRS (-)	f-QRS (+)	
0	175 (87,94)	24 (12,06)	0.002*
1	128 (83,66)	25 (16,34)	
2	67 (80,72)	16 (19,28)	
3	23 (71,88)	9 (28,13)	
4	3 (50,00)	3 (50,00)	
Total	396 (83.72)	77 (16.18)	

* Cochran Armitage Trend Test
QRS fragmentation negative (f-QRS (-)), QRS fragmentation positive (f-QRS (+))

Discussion

This study demonstrated that the prevalence of f-QRS among pregnant women was 16.18 % and the presence of f-QRS was correlated with the number of parity in pregnant women. When the two groups (f-QRS negative group and f-QRS positive group) were compared, no statistically significant difference was observed in terms of clinical echocardiographic parameters.

During pregnancy, a number of changes in the cardiovascular system occur as follows: heart rate, cardiac output and intravascular volume are increased; blood pressure diminishes in the first trimester and returns to its normal level during the third trimester.[9] Incidence of maternal cardiac arrhythmias increases during pregnancy.[10] Although the exact mechanism is not clear; increased plasma volume, increased sympathetic activity and hormonal changes were suspected.[3] Some changes may occur on ECG during pregnancy, such as deviation of the QRS axis, a small Q wave and an inverted P wave in lead III, an increased R/S ratio in leads V2 – V6, changes in the ST segment and T wave.[11] In the literature, some studies suggest that electrocardiographic parameters may be predictive for cardiovascular diseases and poor obstetric prognosis in pregnancy such as P Wave dispersion and QT dispersion.[12] However, there is no information about f-QRS in pregnant women. Fragmented QRS on ECG has been found a marker of myocardial scarring or fibrosis in various diseases.[13] The f-QRS is cheap and readily available electrocardiographic index of myocardial fibrosis. In the pregnancy, which is a physiological condition accompanied by cardiovascular changes, it may be useful to determine easily evaluated parameters in pregnancy in terms of the reaction of pregnant women with cardiac risk in the early period. Based on this hypothesis, we investigated f-QRS in pregnant women and determined that the frequency of fragmentation on rest ECG of pregnant women was 16.18 % (n=77/496). In a previous study, Ying T et all. found that the prevalence of f-QRS in healthy adult was 5.1%.[14] Since there are no studies examining the frequency of fragmentation in the pregnant population in the literature, we found higher prevalence than the general population, making the presence of fragmentation more interesting in this patient group. Additionally, we found higher number of parity in f-QRS positive group than f-QRS negative group and there was a statistically significant trend between fragmentation frequency and parity number. Previous epidemiological studies suggest that multiparity (multiple pregnancies) increases the risk of cardiovascular disease.[15] The mechanisms underlying these findings remain to be elucidated.[16] The mechanism of the association of parity and CVD is not well understood. Estrogen is considered as a protective factor against the developing of CVD. The secretion of estrogen is discontinued during normal pregnancy depending on the reset of ovarian function. More parity and pregnancy mean more exposure to estrogen reduction.[17] Number of parity is also reported to be associated with carotid artery atherosclerosis in elderly women.[18,19]

There is no data as to whether the presence of f-QRS predicts pronounced LV systolic and diastolic dysfunction in pregnant women. In a previous study, the presence of f-QRS on ECG was associated with higher E/E' ratio and lower E' velocity, indicating pronounced diastolic dysfun-

ction among patients with metabolic syndrome.[20] Our study demonstrated that in f-QRS positive group compared to f-QRS negative group, showed a longer deceleration time. Future studies are needed to investigate the clinical significance of this relationship.

In conclusion, the presence of f-QRS was associated with number of parity and we suggest that multiparity may be a risk factor for arrhythmia and other cardiovascular events. Pregnant women with f-QRS on their rest ECG need extra attention in terms of cardiovascular disease. Future studies which investigate association between presence of f-QRS and pregnancy outcomes and clinical significance of f-QRS in pregnancy are needed. This simple tool might help to identify pregnant women who could be at risk for developing overt cardiac dysfunction.

Conclusions

The presence of f-QRS was correlated with increase in number of parity. Pregnant women with f-QRS on their rest ECG need extra attention in terms of cardiovascular disease. By demonstrating clinical significance of f-QRS, this simple tool might be used to determine women who could be at risk for developing cardiac dysfunction in pregnancy.

Limititations

One of the limitations of our study is that we did not assess prospectively association between the presence of f-QRS and pregnancy outcomes. Secondly, since we used echocardiography as imaging method we did not show cardiac fibrosis with other imaging modalities.

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