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Evaluation of f(QRS-T) Angle as a Marker of Coronary Artery Disease Risk in Term Pregnant Women

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ABSTRACT

Objective: An indication of instability in myocardium electrical characteristics is the frontal (QRS-T) [f(QRS-T)] angle. There is a known relationship between this angle and coronary artery disease, such as arrhythmias and sudden death. The purpose of the present study was to investigate the f(QRS-T) angle in term pregnant women and its relationship with advanced maternal age, parity, hemoglobin (Hb), and total blood viscosity.

Methods: A total of 247 term pregnant individuals who had no prior history of cardiac or chronic disease and similar body mess indexes (BMI) were included in the study. Patients were divided into two groups according to their ages: ≥35 and <35 years. f(QRS-T) angles were calculated manually. f(QRS-T) angles, Hb levels, and total blood viscosities were compared between the two groups.

Results: Our study revealed no statistically significant differences in f(QRS-T) angle, Hb levels, or high and low total blood viscosities between the two groups (p>0.05). Additionally, no correlation was found among age, total blood viscosity, and f(QRS-T) angle in term pregnancies with similar gestational weeks and BMI.

Conclusion: The angle of f(QRS-T) is narrower in term pregnancies of women aged ≥35, compared to those under 35, albeit both values fall within normal limits and are unrelated to Hb levels and total blood viscosity. Therefore, regarding this angle, there was no observed increase in extracardiac risk in term pregnancies among women aged ≥35 compared to younger pregnancies.

Keywords: Pregnancy, electrocardiography, blood viscosity

INTRODUCTION

It is possible to forecast future cardiovascular mortality by observing abnormalities in ventricular depolarization and, more specifically, anomalies during the susceptible repolarization period. The spatial QRS-T angle, which is the angle between the directions of ventricular depolarization and repolarization, has been shown in many studies to be predictive of cardiac mortality (1-4). However, most medical professionals are unfamiliar with measuring the spatial QRS-T angle, and currently used computerized electrocardiographic analysis tools do not typically provide this information. On the other hand, the frontal plane QRS-axis and T-wave axis are easily obtained from a typical 12-lead electrocardiogram (ECG) and are typically reported by automated ECG equipment. They make it simple to calculate the f(QRS-T) angle, which has been shown to correlate well with the spatial QRS-T angle for risk prediction (5).

The f(QRS-T) angle is a sign of instability in the myocardium's electrical characteristics. It can be determined by analyzing the absolute difference between the QRS and T axis. The frontal (QRS) angle can be easily calculated from ECG and is an easily accessible and evaluable data that has gained importance in recent years. According to prior research, a relationship between this angle and coronary artery disease has been observed; it is particularly associated with cardiac arrhythmias and sudden cardiac arrest (6-8).

Wide-ranging hemodynamic and hormonal changes occur throughout a typical pregnancy in response to the developing fetus's needs. Although the concept of high-risk pregnancy defined so far has obvious boundaries, in this physiological period, from a cardiac perspective, the f(QRS-T) angle has never been evaluated in term pregnancies. This study aimed to investigate the f(QRS-T) angle in pregnant women aged ≥35 and <35 years, and evaluate its relationship with other parameters that may change cardiac

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load (parity, hemoglobin (Hb) and blood viscosity differences). Therefore, we aimed to identify which pregnancies are associated with a higher risk of arrhythmia and cardiac events by examining this angle and potential related situations. This study is unique and will contribute to the literature.

METHODS

This retrospective cohort study was conducted at the Ankara Bilkent City Hospital, Obstetrics and Gynecology Clinic between June and December 2023. A total of 247 healthy pregnant women were included in the study, and the protocol was approved by the Clinical Research Ethics Committee of Ankara Bilkent City Hospital (decision no: E2-24-6150, date: 24.01.2024). Patients with multiple gestation, abnormal laboratory test results, diabetes mellitus, gestational or pre-gestational hypertension, coronary heart disease, or congenital heart disease were excluded from the study. Patients who had to take any medication, were addicted to drugs, or consumed alcohol or tobacco were also excluded. Patients were divided into two groups: ≥35 and <35 years. The commonly accepted threshold for advanced maternal age (AMA) in the literature is 35 years and older (9,10).

After the patients had rested for 10 minutes in the supine posture, the electrodes were positioned in standard anatomical positions to capture the ECG at a speed of 25 mm/s and a width of 10 mm/mV (Cardiofax M Model ECG -1250; Nichon Kohden Corporation, Tokyo, Japan). The absolute difference between the QRS and T axis, which can be easily acquired from digital ECG data, was used to determine the f(QRS-T) angle. The predicted f(QRS-T) angle from an autonomously produced surface ECG record is shown in Figure 1. The f(QRS-T) angle was determined as 360° minus the absolute difference between the f(QRS-T) and T axes if the difference was greater than 180°. One of the authors, a cardiologist, assessed the f(QRS-T) angles (Figure 1).

The complete blood viscosity was calculated using pre-approved formulas using hematocrit and total plasma protein concentrations at both high cutting rate [high shear rate (HSR) =208/s] and low cutting speed [low shear rate (LSR) =0.5/s]. The formula for whole blood viscosity for HSR (208/s) is as follows: (0.12 × hematocrits) + 0.17 (total protein – 2.07) and whole blood viscosity for LSR (0.5/s): (1.89 × hematocrit) + 3.76 (total protein- 78.42). Here, hematocrit was calculated as %s, total protein concentration as g/L, and whole blood viscosity from the centipoise (cP).

Statistical Analysis

For statistical analysis, SPSS for Windows 18.0 was used (IBM, Chicago, IL, USA). The significance levels of the tests were reported as follows: for normally distributed data, mean ± standard deviation was provided, whereas for non-normally distributed data, the median (minimum-maximum) was reported. The numerical values were examined for normality using the Kolmogorov-Smirnov test. Values with a normal distribution were compared using the Student's t-test, whereas values with a non-normal distribution were compared using the Mann-Whitney U test. For correlation analysis, bivariate Pearson's test was performed. $P<0.05$ was considered statistically significant.

RESULTS

Table 1 shows the demographic, laboratory, and ECG data of 247 term pregnant women divided into groups 1 and 2. As shown in Table 1, no significant differences were observed between maternal age and f(QRS-T) angle.

Subsequently, an analysis was conducted to determine the correlation between blood viscosity and age. As illustrated in Table 2, no correlation was found among blood viscosity, age, and f(QRS-T) angle in term pregnancies with similar gestational weeks and BMI.

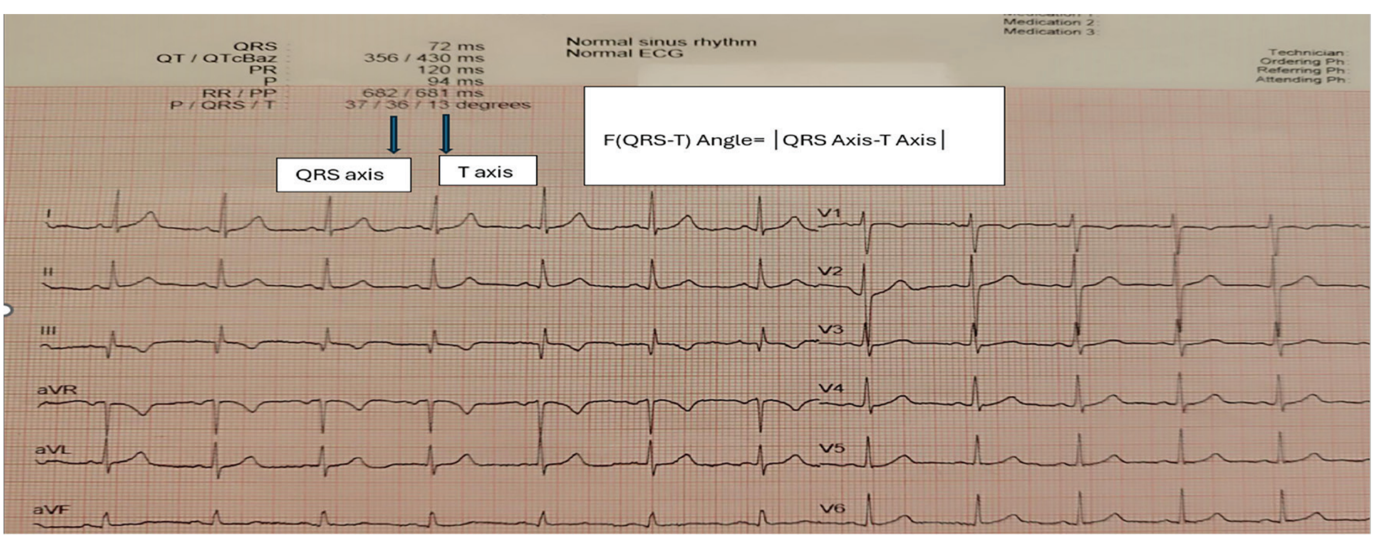

Figure 1. Calculation of the frontal QRS-T angle from the automatic report of surface ECG
ECG: electrocardiogram, f(QRS-T): frontal QRS-T

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DISCUSSION

According to our study, the f(QRS-T) angle was narrower in term pregnancies of women aged 35 years and older than in those under 35 years, although both measurements fell within normal ranges and showed no correlation with Hb levels or total blood viscosity. Consequently, there is no discernible elevation in extracardiac risk in term pregnancies in women aged 35 years and older compared with younger pregnancies.

Table 1. Demographics, laboratory test results, and f(QRS-T) angle findings of group 1 and 2

Parameters	Group 1 n=187	Group 2 n=60	p-value
Parity	1 (0-3)	2 (0-4)	<0.001*
Gestational week	38 (37-41)	38 (37-41)	0.068
Body mass index	28 (25-31)	29 (27-30)	0.008
f(QRS-T) angle	18 (0-73)	15.5 (0-76)	0.756
Hemoglobin (g/dL)	11.55±1.26	11.6±1.28	0.714
Hematocrit, %	35.59±3.76	35.58±3.72	0.988
Total protein level, g/dL	62.3±3.92	61.3±4.08	0.091
Albumin, g/dL	37 (33-44)	36 (31-44)	0.017
Total blood viscosity, HSR, cP	14.5±0.82	14.34±0.78	0.192
Total blood viscosity, LSR, cP	51.16 (3.69-69.34)	51.36 (35.52-66.85)	0.474

*P<0.05 was considered statistically significant. HSR: high shear rate, LSR: low shear rate, cP: centipoise, f(QRS-T): frontal QRS-T
The significance levels of the tests were reported as follows: for normally distributed data, mean ± standard deviation was provided, whereas for non-normally distributed data, the median (minimum-maximum) was reported.

The orientation difference between ventricular depolarization and repolarization is known as the f(QRS-T) axis angle. This represents shifts in the length of the regional action potential and the orientation of the normalization process. Deviations from this metric suggest modified ventricular repolarization associated with underlying anatomical and functional modifications to the heart. As a result, an abnormal f(QRS-T) angle indicates an increased risk of cardiovascular disease (CVD) and all-cause mortality (1,3,4,6,8).

The f(QRS-T) angle varies by gender and age, with women generally having a smaller angle at baseline and widening with age. However, in a study conducted with healthy participants, the upper limits of normal were determined to be between 45° and 60° (6). In a 2012 cohort study of elderly patients considered not to have CVD, the top limits of normality, unique to sex, were 39° for women and 81° for men (11). According to Jogu et al. (12), an abnormal f(QRS-T) angle (for women >104° on the ECG) offers significant predictive data about the likelihood of atrial fibrillation in the elderly (12). An increased risk of arrhythmic death was observed by Aro et al. (8) when the f(QRS-T) angle was more than 100°. As a result, a wide range of factors have been related to cardiac mortality in the general population and are thought to be signs of heterogeneity in ventricular repolarization.

Throughout a typical pregnancy, a wide range of hemodynamic and hormonal changes occur in response to the requirements of the developing fetus. The compensatory physiological adjustments that begin in the initial trimester substantially affect the maternal cardiovascular system. These adjustments encompass a reduction in peripheral vascular resistance alongside an increase in plasma volume, heart rate, and cardiac output (13). Specifically, pregnancy-induced hemodynamic and hormonal alterations influence the maternal heart, potentially leading to eccentric hypertrophy characterized by the enlargement of cardiac cavities and increased left ventricular wall thickness and mass (14). Cardiac remodeling, heightened sympathetic nervous system

Table 2. Correlation analysis between demographic and laboratory test results and f(QRS-T) angle findings of 247 pregnant women

	Age	Parity	Gestational week	BMI	f(QRS-T) angle	Hb	Total protein	HSR, cP	LSR, cP
f(QRS-T) angle	r=0.039 p=0.543	r=0.052 p=0.417	r=0.048 p=0.452	r=0.025 p=0.696	r=1	r=-0.024 p=0.711	r=0.011 p=0.864	r=-0.027 p=0.673	r=-0.018 p=0.776
Hemoglobin (g/dL)	r=0.104 p=0.101	r=0.026 p=0.689	r=0.034 p=0.591	r=0.073 p=0.255	r=-0.024 p=0.711	r=1	r=-0.080 p=0.208	r=0.423* p=0.000	r=-0.308* p=0.000
Hematocrit, %	r=0.098 p=0.123	r=0.012 p=0.851	r=-0.040 p=0.535	r=0.067 p=0.294	r=-0.061 p=0.344	r=0.821 p=0.000	r=-0.045 p=0.486	r=0.559* p=0.000	r=0.424* p=0.000
Total protein level, g/dL	r=-0.164 p=0.010	r=-0.019 p=0.764	r=-0.009 p=0.891	r=0.014 p=0.831	r=0.111 p=0.864	r=-0.080 p=0.208	r=1	r=0.803* p=0.000	r=0.886* p=0.000
Albumin, g/dL	r=-0.137 p=0.303	r=-0.004 p=0.946	r=0.001 p=0.990	r=0.035 p=0.588	r=-0.171 p=0.007	r=0.093 p=0.145	r=0.548* p=0.000	r=0.461* p=0.000	r=0.502* p=0.000
Total blood viscosity, HSR, cP	r=-0.077 p=0.225	r=-0.009 p=0.891	r=-0.031 p=0.629	r=0.051 p=0.422	r=-0.027 p=0.673	r=0.423* p=0.000	r=0.803* p=0.000	r=1	r=0.988* p=0.000
Total blood viscosity, LSR, cP	r=-0.103 p=0.106	r=-0.012 p=0.853	r=-0.026 p=0.681	r=0.043 p=0.496	r=-0.018 p=0.776	r=-0.308* p=0.000	r=0.886* p=0.000	r=0.988* p=0.000	r=1

r: correlation coefficient, BMI: body mass index, HSR: high shear rate, LSR: low shear rate, cP: centipoise, Hb: hemoglobin, f(QRS-T): frontal QRS-T activity, and pregnancy-related hormonal shifts may predispose patients to proarrhythmic effects (15). Notably, arrhythmic events were the third most common etiology of cardiovascular-related mortality, accounting for 22.2% of maternal mortality during and after pregnancy (16). Maternal Hb levels physiologically decrease throughout pregnancy due to hemodilution. The third trimester is when this impact reaches its peak (17,18). Studies conducted during this period revealed no change in plasma viscosity when physiological hemodilution and hypercoagulability were detected in low-risk pregnancies. However, plasma viscosity was observed to increase in pregnancy-induced hypertension or complicated pregnancy outcomes at the time of their delivery (19-21). Under the 2019 American College of Cardiology/American Heart Association guidelines on the primary prevention of CVD, conditions like early menopause, polycystic ovary syndrome, rheumatologic disorders, and unfavorable pregnancy outcomes are considered risk enhancers due to their significance regarding sex-specific or sex-predominant risk markers (22).

Despite extensive research on the negative effects of AMA and delay in childbirth on unfavorable maternal and perinatal outcomes, the definition of AMA remains unclear. This phrase, which is frequently applied to women over 35, describes the latter years of a woman's reproductive life span (9,10). Over-35-year-old pregnant women are at an increased risk of two- to three-fold higher rates of hospitalization, cesarean delivery, and other pregnancy-related complications due to the significant rise in the prevalence of coexisting conditions with aging, such as diabetes, obesity, cancer, and cardiovascular, renal, and autoimmune diseases (23-26). In this study, we conducted a comparative analysis between term pregnancies in women aged ≥35 and those aged <35 years. Our study revealed no statistically significant differences in f(QRS-T) angle, Hb level, or high and low total blood viscosities between the two age groups. Furthermore, we observed no statistically significant differences after evaluating these parameters, regardless of maternal age. This suggests that the physiological hemodynamic and hormonal changes occurring during pregnancy, regardless of AMA or not, do not lead to significant alterations in the f(QRS-T) angle in low-risk term pregnancies. In addition, our analysis revealed the absence of a significant correlation between Hb, hematocrit, blood viscosity, and f(QRS) angle value in pregnant women in all term, irrespective of age.

Study Limitations

The retrospective nature of this study necessitated a limited sample size, which is considered a limitation of the study.

CONCLUSION

In conclusion, assessing the f(QRS-T) angle showed that AMA did not result in supplementary cardiac risk compared with younger pregnancies.

Ethics Committee Approval: The Clinical Research Ethics Committee of Ankara Bilkent City Hospital approved the study protocol (decision no: E2-24-6150, date: 24.01.2024).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

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Conflict of Interest: The authors have no conflict of interest to declare.

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