

The Relationship Between the Frontal QRS-T Angle and High Blood Pressure Response to Exercise

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ABSTRACT

Introduction: In this study, we compared frontal QRS-T angles between normotensive subjects with high blood pressure (BP) response to exercise test and the control group.

Methods: Patients who were scheduled for an exercise test between January 2017 and January 2022 were included in the study. The patient group consisted of people who responded to the exercise test with elevated BP, and the control group included people who responded to the exercise test with normal BP. The data in the electrocardiography device's report section was used to calculate the QRS and T-axis. The frontal QRS-T angle was identified as the absolute difference between these two axes.

Results: Frontal QRS-T angles were found to be significantly higher in the patient group compared with the control group (36.09 ± 14.51 and 20.46 ± 8.12 ; $p < 0.001$). In multivariate analysis, frontal QRS-T angles were found to be an independent predictor of higher BP response to exercise test [odds ratio: 1,189, 95% confidence interval (CI); 1,083-1,305; $p < 0.001$]. Receiver operating characteristic curve analysis showed that the frontal QRS-T angle value predicting an excessive BP response to exercise test was 27.5° with a sensitivity of 71% and a specificity of 75% (area under the curve: 0.832; 95% CI: 0.75-0.91; $p < 0.001$).

Conclusion: The frontal QRS-T angles were found to be significantly higher in the group that gave higher BP response to the exercise test compared to the control group. Patients with a high BP response to exercise test can be detected using the frontal QRS-T angle before the test.

Keywords: Hypertension, exercise test, excessive blood pressure response, F (QRS-T)

Introduction

Hypertension (HT) is one of the most common preventable cardiovascular risk factors (1-3). An increase in the prevalence of HT is observed with the aging population, and it is predicted that it will affect approximately 1.5 billion people worldwide by 2025. HT is a global public health problem that causes end-organ damage, leading to complications such as myocardial infarction, cerebrovascular disease, and renal failure because of delays in early diagnosis and treatment (4). The exercise test is a non-invasive, inexpensive, and easy diagnostic method used by clinicians for many years to assess the effectiveness and functional capacity of the therapy applied in the diagnosis of cardiovascular diseases (5). During the exercise test, blood pressure (BP) and electrocardiography (ECG) recordings were taken at the initial stage and all stages of the test. During exercise, BP increases because of the rise in cardiac output that occurs to fulfill the increased metabolic requirements of the body. In some individuals, BP rises excessively during exercise, and systolic BP increases

to 210 mmHg or more in males and 190 mmHg or more in women. This group is considered to be patients with an excessive hypertensive response to exertion (6). The response to high BP that occurs when exercising is multifactorial and its mechanism is unclear. The higher BP response to exercise has been associated with endothelial dysfunction, increased vascular resistance, and morphological abnormalities of peripheral arteries (7,8). Patients who are normotensive before the exercise test and who experience an excessive BP response during the test are at risk of developing HT during subsequent follow-up, according to research (9). Patients in the Framingham Heart Study who had an elevated BP response after an exercise test developed HT during their 8-year follow-up (10).

The surface ECG measurements QT dispersion (QTd) and Tp-e interval demonstrate the heterogeneity of ventricular repolarization. The literature has demonstrated that individuals with HT have longer QTd and Tp-e intervals, which demonstrate cardiac repolarization heterogeneity (11-



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13). Recently, a novel ECG measure called frontal QRS-T angles has been employed to demonstrate ventricular repolarization heterogeneity. It is easily calculable using data from ECG and known as the angle between the QRS and T-axis. The association between various diseases and QRS-T angle has been demonstrated in earlier investigations (14-17).

Previous studies have examined how QRS-T angle and HT are related. We compared the frontal QRS-T angle, which depicts ventricular repolarization heterogeneity, between participants who responded to the exercise test with elevated BP and a control group.

Methods

Patient population: The study included patients who visited the cardiology clinic between January 2017 and January 2022 and underwent a treadmill exercise test. Excessive hypertensive response to exertion was defined as systolic BP increase of 210 mmHg or more in men and 190 mmHg or more in women (6). The patient group consisted of people who responded to the exercise test with elevated BP, and the control group included people who responded to the exercise test with normal BP. Retrospective reviews of patient data, laboratory results, and electrocardiographic parameters were performed using hospital information system data. The following patients were excluded from the current study: Those with a history of HT or taking antihypertensive medication, those with a history of diabetes, those with severe valve pathology, left ventricular hypertrophy, those taking oral contraceptives, hormone replacement therapy, or steroids, those with known coronary artery disease, cancer, thyroid dysfunction, or those who were pregnant at the time of diagnosis. The University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Local Ethics Committee approved the study protocol (approval number: 2022-10-07, date: 23.05.2022).

Echocardiography: The same cardiologist who evaluated the patients for our study used the EPIQ 7C, S5-1, and X5-1 transducer from Philips Healthcare (Andover, Massachusetts). Before the surgery, the patients were placed in the left lateral decubitus position. By the standards of the American Society of Echocardiography recommendations, imaging was carried out through the parasternal long and apical windows (18). This research excluded patients with significant valve pathology, left ventricular hypertrophy, and heart failure.

Frontal QRS-T angle: All patients underwent 12-lead ECG using the (Mortara Instrument ELI 250) equipment in the supine position at a speed of 25 mm/s and voltage of 10 mm/mv before the exercise test, after resting for at least 15 min. With the use of a magnifying lens, the same cardiologist computed each measurement. The data in the ECG device's report section were used to calculate the QRS and T-wave axis. The frontal QRS-T angle was identified as a difference between the QRS and T-axis. Figure 1 shows the frontal QRS-T angle calculation method.

Exercise stress test: Exercise stress testing was performed on research participants using the Bruce protocol (Schiller, Cardiovit Cs-200). Throughout the test, the patient's BP and ECG were checked and recorded every three minutes. BP readings below 210 mmHg for males and 190 mmHg for women were deemed excessive BP responses to exertion (12). The exercise test was stopped if the heart rate was exceeded by more

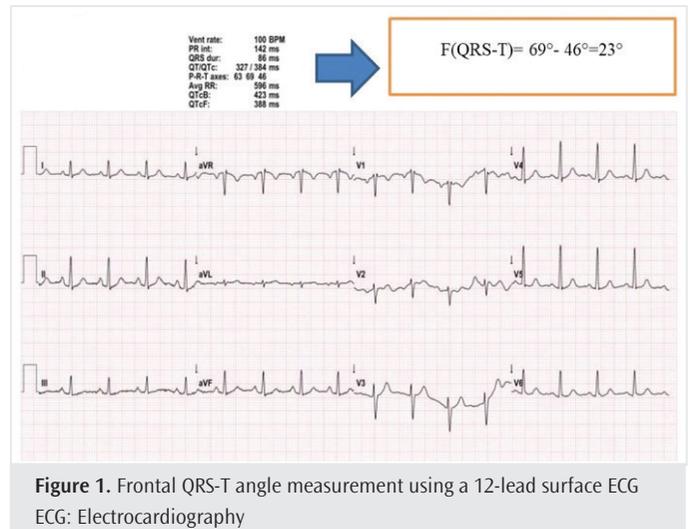


Figure 1. Frontal QRS-T angle measurement using a 12-lead surface ECG: Electrocardiography

than 85% of the target heart rate, if the ECG recordings revealed ischemia abnormalities, if the systolic BP dropped by more than 10 mmHg, or if the patient requested that the test be stopped because of a complaint.

Biochemical parameters: Biochemical parameters of the patients were measured using the AU5800 Clinical Chemistry System (Beckman Coulter, INC, California, USA) device, and hematological parameters with the XT-4000i Hematology Analyzer (Sysmex, Kobe, Japan). A BP Holter device was used to measure 24-h ambulatory BP in all trial participants (Suntech, Bravo 24-HR ABP), and white-coat HT was eliminated.

Statistical Analysis

All statistical analysis was performed using the NCSS 2007 (Kaysville, Utah, USA). The Independent sample t-test and the Mann-Whitney U test were used to analyze the study data. The Independent sample t-test was used to compare normally distributed parameters, and the Mann-Whitney U test was used to compare non-normally distributed parameters between the patient and control groups. Comparing qualitative data was performed using the pearson chi-square test. To ascertain the impacts on risk categories, a multivariate analysis was conducted. The cut-off value was determined using receiver operating characteristic analysis. Statistical significance was assessed at the $p < 0.01$ and $p < 0.05$ levels.

Results

Basic demographic and laboratory findings: Table 1 presents the demographic details of the research participants. A total of 101 participants were included, of whom 53 were the control group and 48 showed high BP response to the exercise test (patient group). The mean age was 47.23 ± 9.28 in the patient group and 45.07 ± 7.76 years in the control group ($p = 0.663$). Body mass index (BMI) was different between the two groups (27.34 ± 2.32 and 23.2 ± 1.95 ; $p = 0.021$). In Table 2, laboratory data comparisons are shown. The white blood cell count was substantially greater in the patient group when the hematological parameters were analyzed (7.51 ± 1.48 and 7.38 ± 2.01 ; $p < 0.001$). Serum HDL levels were substantially lower in the patient group compared with the control group (43 ± 8.01 and 54.83 ± 12.28 ; $p < 0.001$).

ECG findings: Table 3 shows the comparison of the heart rates, PR duration, QRS duration, and frontal QRS-T angle between the patient and control groups using ECG measurements. The frontal QRS-T angle in the patient group was found to be substantially wider than in the control group (36.09 ± 14.51 and 20.46 ± 8.12 ; $p < 0.001$). Other ECG parameters across the two groups did not significantly differ from one another. BMI [odds ratio (OR): 2.63; 95% confidence interval (CI): 1,517-4,559; $p < 0.001$] and QRS-T angle (OR: 1,189; 95% CI: 1,083-1,305; $p < 0.001$) independently predicted patients with high BP in the multivariate logistic regression analysis (Table 4). As a result, individuals with high BP who responded to exercise were predicted to have a frontal QRS-T angle

$\geq 27.5^\circ$ with 71% sensitivity and 75% specificity (area under the curve: 0.831; 95% CI: 0.75-0.91; $p < 0.001$) (Figure 2, Table 5).

Discussion

The frontal QRS-T angle is simple to measure using a surface ECG. The frontal QRS-T angle was considerably higher in patients who responded to the exercise test with higher BP in comparison to the control group, which was the major finding. To the best of our knowledge, this study is the first to demonstrate a relationship between the frontal QRS-T angle and elevated BP response to exercise.

Table 1. Comparison of the basic demographic and clinical characteristics between the groups

Variables	Patient group (n=48)	Control group (n=53)	p-values
Gender, male, n (%)	21 (43.8)	26 (49.1)	0.593
Age, years	47.23 ± 9.28	45.07 ± 7.76	0.663
Body mass index	27.34 ± 2.32	23.2 ± 1.95	0.001
Smoking, n (%)	11 (22.9)	10 (18.8)	0.236
Rest BP, mmHg			
Systolic	125 ± 12	122 ± 16	0.142
Diastolic	78 ± 8	76 ± 10	0.211
Maximum BP during exercise, mmHg			
Systolic	212 ± 24	187 ± 28	0.001
Diastolic	94 ± 10	88 ± 12	0.041
Proportion achieving target heart rate	34 (70)	48 (90)	0.022
Exercise capacity and metabolic equivalents	7.4 ± 2.1	10.3 ± 3.2	0.043

BP: Blood pressure

Table 2. Comparison of laboratory parameters between the groups

Variables	Control group, (n=53)	Patient group, (n=48)	p-values
Glucose, (mg/dL)	94.15 ± 14.26 (93)	95.2 ± 9 (92.5)	0.529
Creatinine, (mg/dL)	0.85 ± 0.13 (0.87)	0.69 ± 0.1 (0.68)	0.200
AST, (IU/L)	22.47 ± 12.95 (22)	17.07 ± 4.02 (17)	0.466
ALT, (IU/L)	23.7 ± 15.03 (21)	15.68 ± 5.82 (15)	0.500
Total cholesterol, (mg/dL)	193.38 ± 36.54 (192)	200.28 ± 38.49 (205)	0.511
Triglycerides, (mg/dL)	172.62 ± 97.15 (148)	139.11 ± 82.41 (108.5)	0.960
LDL, (mg/dL)	119.51 ± 44.4 (111)	117.26 ± 33.67 (121)	0.836
HDL, (mg/dL)	54.83 ± 12.28 (54.5)	43 ± 8.01 (42)	0.001
White blood cells ($10^3/\mu\text{L}$)	7.38 ± 2.01 (7.18)	7.51 ± 1.48 (7.15)	0.001
Hemoglobin, (g/L)	15.25 ± 1.14 (15.2)	13.1 ± 1.22 (13.2)	0.701
Thrombocyte, ($10^3/\mu\text{L}$)	242.15 ± 66.51 (235)	273.67 ± 63.73 (270)	0.450

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

Table 3. Comparison of the electrocardiographic parameters between the groups

Variables	Control group, (n=53)	Patient group, (n=48)	p-values
Heart rate	77.13 ± 11.97	79.45 ± 12.98	0.353
QRS time (ms)	90.48 ± 9.26	90.74 ± 11.62	0.903
PR interval (ms)	152.65 ± 21.27	147.68 ± 17.86	0.205
P wave (ms)	96.65 ± 5.62	97 ± 5.49	0.750
Frontal QRS-T angle ($^\circ$)	20.46 ± 8.12	36.09 ± 14.51	0.001

Table 4. Multivariate analysis of independent predictors of excessive BP response to the exercise test

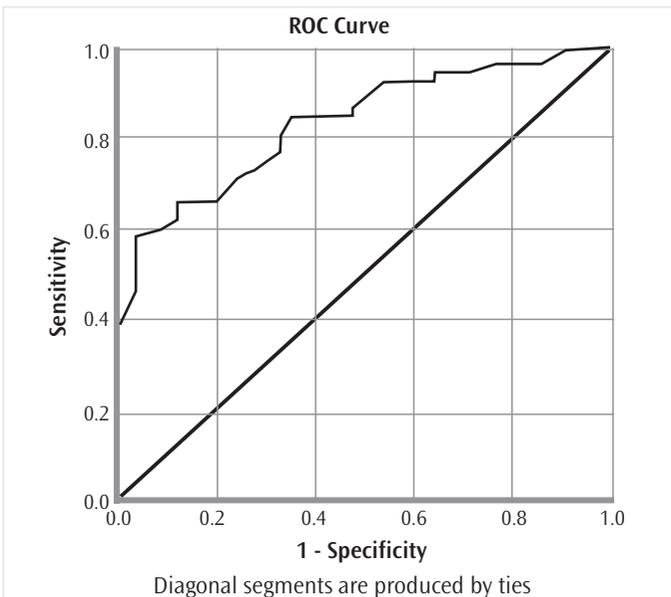
	Odd's ratio	95% Confidence interval		p-values
		Lower	Upper	
Body mass index	2,630	1,517	4,559	0.001
HDL	1,012	0.950	1,078	0.710
Frontal QRS-T angle	1,189	1,083	1,305	0.001
White blood cell	22,213	1,887	261,496	0.014
Neutrophil	0.015	0.001	0.677	0.031
Neutrophil/lymphocyte	213,273	4,870	9239.389	0.005

BP: Blood pressure, HDL: High-density lipoprotein

Table 5. ROC analysis of the frontal QRS-T angle

	Cut-off value	AUC	Sensitivity	Specificity	95% confidence interval	
					Lower	Upper
Frontal QRS-T angle (°)	≥27.50	0.831	0.717	0.750	0.754	0.910

ROC: Receiver operating characteristic, AUC: Area under the curve

**Figure 2.** ROC curve analysis of the frontal QRS-T angle in predicting the excessive BP response to the exercise test

ROC: Receiver operating characteristic, BP: Blood pressure

Studies on normotensive groups without a history of HT but with an excessive BP response during an exercise test have also been conducted (18). In healthy subjects performing the test, there is a progressive increase in BP brought on by an enhanced cardiac output. However, during the exercise test, some individuals with confirmed normotension experience an abnormal rise in BP. According to studies in the literature, the group with an excessive BP response during the exercise test is more likely to develop HT during their follow-up (19). The high BP response to the exercise test group in the CARDIA trial, which comprised 3,741 young adults with normotension, was linked to the onset of HT over a 5-year follow-up (20). Similar to this, participants in the 8-year-long Framingham Heart Study who had an elevated BP response to exercise were linked to the emergence of HT (10). It is well known that with an increase in the BMI, the prevalence of HT also increases. The mean BMI

was found to be 26.8 kg/cm² in the PATENT research, which was carried out to determine the prevalence of HT in our country (21). BMI and non-dipper HT were shown to be correlated in a study of 269 people with newly diagnosed HT (22). BMI is a reliable predictor of the higher QRS-T angle (23). Similar to previous studies, the BMI was a predictor of QRS-T angle in our study.

The angle difference between the QRS and T waves, which is used to determine QRS-T angle, is a novel measure of the heterogeneity of cardiac repolarization (14). Two approaches may be used to compute it. Calculating the QRS-T angle is challenging and needs specialized software however, the surface ECG report section may be used to quickly compute QRS-T angle (24). It has been demonstrated that a QRS-T angle is associated with increased left ventricular mass and poor prognosis (14,25). There are studies in the literature that demonstrate a correlation between the frontal and spatial QRS-T angles. Previous investigations have demonstrated a correlation between the frontal QRS-T angle and coronary artery disease severity. In a study including 1,299 patients who underwent coronary angiography, those with a QRS-T angle greater than 90° had a higher frequency of two or three-vessel disease. A high QRS-T angle was detected in postoperative atrial fibrillation (26). Tanriverdi et al. (27) demonstrated that in individuals without left ventricular hypertrophy, QRS-T angle was higher in the non-dipper hypertensive group than in the dipper group. Bağcı and Aksoy (28) revealed that in pre-hypertensive patients, QRS-T angles were higher than in normotensive individuals. Collagen deposition in myocytes has been shown in pre-HT. Fibrosis leads to disruption of the homogenous structure of the ventricle (29). Echocardiographic imaging can not exclude pathological myocardial fibrosis.

Study Limitations

The relationship between patients with high BP reaction to an exercise test and frontal QRS-T angle requires more research with larger patient populations and longer-term follow-up. However, there was no study conducted on the relationship between excessive BP response and QRS-T angle.

Conclusion

ECG measurements may be crucial in identifying individuals who are at risk of developing HT in the future. Cardiovascular events may be avoided by early identification of individuals who are predisposed to developing HT and early initiation of antihypertensive medication. To support these results, larger and more randomized controlled investigations are required.

Ethics Committee Approval: The University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Local Ethics Committee approved the study protocol (approval number: 2022-10-07, date: 23.05.2022).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions: Concept - F.B., S.Ç., A.D.; Design - F.B., S.Ç., A.D.; Data Collection or Processing - F.B., S.Ç., A.D.; Analysis or Interpretation - F.B., S.Ç., A.D.; Literature Search - A.D.; Writing - F.B., S.Ç., A.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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