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Frontal QRS-T angle in patients with the suspicion of Coronavirus disease 2019 (COVID-19): could it be used as a predictive gravity sign even before the diagnosis by PCR?

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Abstract. – OBJECTIVE: Coronavirus disease 2019 (COVID-19) has been an ongoing global public health concern, causing serious challenges in diagnosing the disease timely. We investigated the value of the frontal QRS-T (fQRS-T) angle in patients visiting the emergency department with the suspicion of COVID-19.

PATIENTS AND METHODS: A hundred and thirty-seven patients with the complaint of dyspnea were evaluated retrospectively. The patients with a history of coronary artery disease, heart failure, pulmonary disease, hypertension, diabetes mellitus, or using any medication such as heart rate controllers or antiarrhythmic drugs were excluded from the study. The angle between frontal QRS- and T-wave axis was defined as the fQRS-T angle, and the patients were divided into two groups based on the fQRS-T angle (group 1, <90° and group 2, ≥90°). Demographic, clinical, electrocardiographic data and rRT-PCR results were compared between the groups.

RESULTS: The mean value of the fQRS-T angle of all participants was 45.26°. There was no significant difference between the groups according to the demographic and clinical data. Subjects with wider fQRS-T angle (group 2) had higher heart rates (p = 0.018), higher corrected QT values (p = 0.017), and higher QRS axis (p = 0.001). The patients in group 2 had a higher number of positive COVID-19 rRT-PCR test results compared to subjects with the normal fQRS-T angle (p = 0.002). In multivariate regression analysis, fQRS-T angle (p = 0.027, OR: 1.013, 95% CI: 1.001-1.024) was found as an independent variable affecting the PCR test results.

CONCLUSIONS: Prompt diagnosis, initiating preventive and protective measures in an early stage of COVID-19 are crucial. In suspected COVID-19 infection, the use of faster-resulting tests and diagnostic tools for COVID-19 allows patients to be diagnosed and treated in a timely manner for recovery, thereby optimizing patient management. Therefore, the fQRS-T angle can be used in patients with dyspnea as a part of diagnostic scores of COVID-19, even before the rRT-PCR test results and overt disease.

Key Words:
COVID-19, Frontal QRS-T angle, Coronavirus.

Introduction

The new coronavirus (COVID-19) is a quickly progressing systemic disease. Even if pulmonary distress is the most significant manifestation, emergency clinicians should be aware of the other systemic complications which can be associated with mortality[1-4]. Research was manly focused on the diagnosis, however, diagnostic tools and tests are not cost-effective and could delay the precise diagnosis and optimal management[5-7].

It was observed that approximately most of the COVID-19 patients are associated with respiratory complications, and almost one-third of them had cardiac involvement, which has been implicated with more severe disease[8,9].

We hypothesized that the frontal QRS-T (fQRS-T) angle, a marker of ventricular repolarization heterogeneity, could be used as a part of diagnostic scores of COVID-19. Therefore, the present study was undertaken to investigate whether there is a relationship between the COVID-19 real-time reverse transcription-polymerase chain reaction (rRT-PCR) test results and the fQRS-T angle, or not.

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Patients and Methods

Patient Selection

We retrospectively analyzed the initial electrocardiography and rRT-PCR test results of patients visiting the emergency department with the clinical suspicion of COVID-19.

A hundred and thirty-seven patients with the complaint of dyspnea were included. The patients with a history of coronary artery disease, heart failure, pulmonary disease, hypertension, diabetes mellitus, or using any medication such as heart rate controllers, or antiarrhythmic drugs were excluded from the study. Demographic, clinical, and electrocardiographic data of the patients were obtained from the medical records. The data were compared between the groups.

12-Lead-Electrocardiography and the Frontal QRS-T (fQRS-T) Angle

A resting electrocardiograhy (ECG) was recorded in the emergency department (25 mm/sec and 10 mm/mV). Automated values were obtained from the ECG machine (Schiller CardoVit AT-2plus, Baar, Switzerland). The absolute difference (angle) between the T-wave axis and the frontal QRS wave axis was defined as the frontal QRS-T angle[10-14]. A trained study technician blinded to COVID-19 status evaluated all ECGs, and confirmed the results. The patients were separated into 2 groups according to the fQRS-T angle: group 1 (normal) = 111 patients with fQRS-T angle of 0-90° and group 2 (abnormal) = 26 patients with fQRS-T angle ≥90°.

Statistical Analysis

SPSS program, version 21 (IBM Corp., Armonk, NY, USA) was used for all statistical measurements and calculations. The Kolmogorov-Smirnov test was used to test for normal distributions. The categorical variables such as the PCR test results were presented as numbers and percentages, and the continuous variables as means ± standard deviations (SD). The categorical data were compared with the Chi-Square test. Significant differences between the groups were determined with the *t*-test. The correlation analysis was used to evaluate the strength of the relationship between patients' data and COVID-19 PCR test results. The parameters with *p*-value less than 0.2 in univariate regression analysis were included in multivariate regression analysis. Multivariate linear regression analysis was performed for the estimation of relationship between COVID-19 PCR test results and independent variables. A *p*-value less than 0.05 was considered statistically significant.

Results

The mean age of all patients was 46.4 ± 15.9 years. Of the 137 cases, 68 (49.6%) were male and 34 (24.8%) were smokers. The mean time of onset of symptoms was 4.8 ± 4.6 days. There were 30 patients (21.90%) with fever, 85 patients (62.04%) with cough, 88 patients (64.23%) with fatigue, 22 patients (16.06%) with diarrhea, 41 patients (29.93%) with chest pain, 61 patients (44.53%) with headache, 16 patients (11.68%) with palpitation, 94 patients (68.61%) with muscle or joint pain, and 21 patients (15.33%) with loss of taste or smell. There was no significant difference between the groups according to the demographic and clinical data.

The mean value of the fQRS-T angle of all participants was 45.26°. The mean values of fQRS-T angle were 28.58° and 116.46° in group 1 and group 2, respectively ($p = 0.000$). Subjects with wider fQRS-T angle (group 2) had higher heart rates ($p = 0.018$), corrected QT ($p = 0.017$) and QRS axis ($p = 0.001$) values.

In our study, COVID-19 was diagnosed based on the PCR test results. The PCR testing was performed in patients with the suspicion of COVID-19 disease, especially with respiratory complaints. The samples were taken from the patient's nose and throat with the cotton swab. The mean time to obtain rRT-PCR test results was two days. COVID-19 rRT-PCR tests resulted positive (+) in 44 patients. Patients in group 2 had a higher number of positive PCR test results compared to subjects with a normal fQRS-T angle ($p = 0.002$). The rRT-PCR (+) patients were prescribed isolation for two weeks and supportive treatment in accordance with the national guidelines.

The demographic, clinical, and electrocardiographic data of all participants and of those with normal (group 1) and abnormal fQRS-T angles (group 2) are illustrated in Table I.

QRS axis, fQRS-T angle, BMI, smoking, and symptoms such as fever, cough, and muscle-joint pain were correlated with PCR test results in the correlation analysis. In multivariate regression analysis, fQRS-T angle ($p = 0.027$, Odds Ratio (OR): 1.013, 95% Confidence Interval (CI): 1.001-1.024) and muscle-joint pain ($p = 0.039$, OR: 0.368, 95% CI: 0.143-0.952) were the independent variables affecting the PCR test results (Table II).

In a receiver operating curve (ROC) analysis, the cut-off level for the fQRS-T angle in predicting the COVID-19 PCR test result was defined as a value greater than 90°. The fQRS-T angle >90° had 70.5% sensitivity and 64.5% specificity (Area under curve (AUC): 0.624; 95% CI: 0.518-0.730; $p = 0.020$) for predicting the PCR test results (Figure 1).

Table I. The demographic, clinical, and electrocardiographic data of all participants.

	Group 1 fQRS-T angle <90° (n=111)	Group 2 fQRS-T angle ≥90° (n=26)	All patients (n=137)	*p*-value
Age, years	45.6 ± 14.9	49.4 ± 20.2	46.4 ± 15.9	0.380
Male	56 (50.5%)	12 (46.2%)	68 (49,6%)	0.696
BMI, kg/m²	26.79 ± 4.02	25.64 ± 4.81	26.57 ± 4.19	0.208
Smoking	26 (23.4%)	8 (30.8%)	34 (24.8%)	0.439
Onset of symptoms, day	4.8 ± 4.3	4.7 ± 5.9	4.8 ± 4.6	0.880
Symptoms				
Fever	24 (21.62%)	6 (23.08%)	30 (21.90%)	0.873
Cough	70 (63.06%)	15 (57.69%)	85 (62.04%)	0.615
Fatigue	75 (67.57%)	13 (50.00%)	88 (64.23%)	0.117
Diarrhea	19 (17.12%)	3 (11.54%)	22 (16.06%)	0.489
Chest Pain	32 (28.83%)	9 (34.62%)	41 (29.93%)	0.565
Headache	53 (47.75%)	8 (30.77%)	61 (44.53%)	0.110
Palpitation	12 (10.81%)	4 (15.38%)	16 (11.68%)	0.117
Muscle-joint pain	76 (68.47%)	18 (69.23%)	94 (68.61%)	0.940
Loss of taste/smell	18 (16.22%)	3 (11.54%)	21 (15.33%)	0.555
Electrocardiographic data				
Heart rate, bpm	80.75 ± 14.78	88.81 ± 18.19	82.28 ± 15.68	**0.018**
PR, msec	152.34 ± 22.92	156.00 ± 22.16	152.99 ± 22.67	0.477
QRS, msec	90.83 ± 11.56	91.23 ± 12.38	90.91 ± 11.63	0.875
QTc, msec	399.34 ± 17.36	408.77 ± 19.85	401.13 ± 18.10	**0.017**
P axis°	53.06 ± 27.29	61.42 ± 25.19	54.57 ± 26.92	0.171
QRS axis°	31.90 ± 35.13	-10.08 ± 57.14	23.93 ± 43.10	**0.001**
T axis°	40.96 ± 26.94	11.62 ± 71.88	35.39 ± 40.72	0.050
Frontal QRS-T angle°	28.58 ± 22.65	116.46 ± 22.29	45.26 ± 41.11	**0.000**
COVID-19 PCR test (+)	28 (25.2%)	16 (61.5%)	44 (32.1%)	**0.002**

Values are given as means ± SD or n (%). BMI, body mass index; QTc, corrected QT.

Table II. Relationships between numerous variables and PCR test results, and effects of variables on the PCR test results.

	Correlation analysis		Multivariate regression analysis		
	r	*p*-value	*p*-value	OR	95% CI
BMI	0.153	0.075	0.100	–	–
Smoking	-0.106	0.219	0.080	–	–
Fever	0.127	0.139	0.094	–	–
Cough	0.151	0.077	0.067	–	–
Muscle-joint pain	0.128	0.135	**0.039**	0.368	0.143- 0.952
QRS axis	-0.301	**0.000**	0.073	–	–
fQRS-T angle	0.251	**0.003**	**0.027**	1.013	1.001- 1.024

OR, odds ratio; CI, confidence interval.

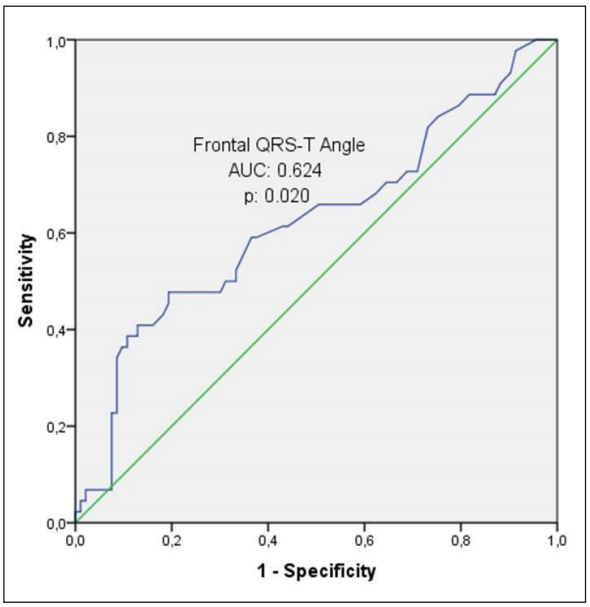

Figure 1. A receiver operating curve analysis of frontal QRS-T angle in predicting PCR test results (AUC: Area under curve).

Discussion

In the present study, we found that positive COVID-19 rRT-PCR test results were statistically higher in patients with wider fQRS-T angle (≥90°). Our data also demonstrated that the fQRS-T angle, with high specificity and sensitivity levels, could be used as a part of diagnostic tools in predicting rRT-PCR test results in patients with the suspicion of COVID-19.

COVID-19 is a systemic illness with multiorgan involvement and is characterized by hyperinflammation[1-4,8,9]. Most of the cases are asymptomatic, however, the contagiousness of the disease is very high, and it is very important for the patients with a high susceptibility to symptomatic infection[2]. Considering the absence of an effective treatment, identifying and isolating infected patients seems to be the most available methods to reduce disease transmission[1,7-10]. Diagnostic testing for COVID-19 is dependent on the availability, cost-effectiveness, and timing to obtain the results. As for now, the gold standard test for the diagnosis of COVID-19 is rRT-PCR[5,6]. Due to its high diagnostic accuracy, it can differentiate the virus at an early stage of disease when the viral load is lowest. rRT-PCR results of COVID-19 are generally available within a few hours, however, the delay in obtaining the results due to the transportation of specimens, and the requirement of specimens in a large run increase the risk of disease transmissibility[5,6].

The absolute difference between the frontal QRS axis and T axis, fQRS-T angle, can be obtained from a surface electrocardiography[11-13]. It has been reported that the wide fQRS-T angle (>90°) could be regarded as a marker of ventricular repolarization heterogeneity, and wider fQRS-T angle was associated with a higher risk of cardiovascular mortality and sudden death[14-16].

Even respiratory complaints are the major clinical manifestation of the disease, approximately 30% of the patients develop a cardiac injury, due to inflammation, stress, and viral invasion of cardiomyocytes[8]. Chen et al[17] reported that the virus may cause direct damage *via* angiotensin-converting enzyme-2 receptors located within the cardiac tissue. Cardiac complications including myocarditis, heart failure, and coronary syndromes could be observed in COVID-19 patients with or without prior cardiovascular disease.

Kurisu et al[18] mentioned that the fQRS-T angle was associated with cardiac diastolic function in the absence of significant perfusion abnormality. In a recent review, Haseeb et al[19] recommended that new electrocardiographic changes associated with the clinical presentation could be considered to be a marker of cardiac involvement of the COVID-19. Recently, Yenerçağ et al[20] found a significant change in ventricular repolarization parameters in COVID-19 patients.

We believe that widening of the fQRS-T angle in COVID-19 patients could reflect the cardiac involvement of COVID-19. This involvement could be characterized by the change in the electrical activity of myocardium, thereby resulting in cardiac diastolic dysfunction and dyspnea, even before the overt disease. Therefore, it is crucial to assess and observe the ECG alterations in the context of COVID-19 paving way for an urgent action. COVID-19 suspected patients with wide fQRS-T angle should be immediately treated as suspects of potential serious COVID-19 cardiac expressions, even before the diagnosis is made by PCR.

Conclusions

Diagnosis and applying preventive and protective measures in an early stage of COVID-19 are very important. In suspected infection, the use of faster-resulting, inexpensive, and non-invasive tests and diagnostic tools for COVID-19 allows

patients to be diagnosed and treated in time for recovery, thereby optimizing patient management. Therefore, fQRS-T angle can be used in patients presenting with dyspnea as a part of diagnostic scores of COVID-19, even before the rRT-PCR test results and overt disease.

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

Ethics Approval
The study has complied with the principles outlined in the Declaration of Helsinki, and the Local Ethics Committee approved the study protocol (E.31808, 20/330).

Informed Consent
Informed consent was not required due to the retrospective nature of the study.

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Authors' Contribution
E.Y., S.D., and E.C. were involved in planning and supervised the work. E.Y. and S.D. processed the data, performed the analysis, drafted the manuscript and designed the figure. E.Y. and T.C. aided in interpreting the results and worked on the manuscript. All authors read and approved the final version of the manuscript.

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Data Availability
The data supporting this article is available from the corresponding author on reasonable request.

References

1) Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, Brown TS, Der Nigoghossian C, Zidar DA, Haythe J, Brodie D, Beckman JA, Kirtane AJ, Stone GW, Krumholz HM, Parikh SA. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. J Am Coll Cardiol 2020; 75: 2352-2371.
2) Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med 2020; 38: 1504-1507.
3) Bijlani R. The COVID-19 pandemic as an opportunity for advances in medicine. Natl Med J India 2020; 33: 316.
4) Shakoori TA, Hafeez MM, Malik A. Could COVID-19 Be a Hemoglobinopathy? Acta Clin Croat 2020; 59: 740-744.
5) Younes N, Al-Sadeq DW, Al-Jighefee H, Younes S, Al-Jamal O, Daas HI, Yassine HM, Nasrallah GK. Challenges in Laboratory Diagnosis of the Novel Coronavirus SARS-CoV-2. Viruses 2020; 12: 582.
6) Shrestha LB, Pokharel K. Standard Operating Procedure for Specimen Collection, Packaging and Transport for Diagnosis of SARS-COV-2. JNMA J Nepal Med Assoc 2020; 58: 627-629.
7) Trivedi N, Verma A, Kumar D. Possible treatment and strategies for COVID-19: review and assessment. Eur Rev Med Pharmacol Sci 2020; 24: 12593-12608.
8) Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020; 323: 1239-1242.
9) Atik D, Kaya HB. Evaluation of the Relationship of MPV, RDW and PVI Parameters With Disease Severity in COVID-19 Patients. Acta Clin Croat 2021; 60(1): 103-114.
10) Wang H, Wei R, Rao G, Zhu J, Song B. Characteristic CT findings distinguishing 2019 novel coronavirus disease (COVID-19) from influenza pneumonia. Eur Radio 2020; 30: 4910-4917.
11) Gungor M, Celik M, Yalcinkaya E, Polat AT, Yuksel UC, Yildirim E, Firtina S, Bugan B, Ozer AC. The Value of Frontal Planar QRS-T Angle in Patients without Angiographically Apparent Atherosclerosis. Med Princ Pract 2017; 26: 125-131.
12) Lazzeroni D, Bini M, Camaiora U, Castiglioni P, Moderato L, Ugolotti PT, Brambilla L, Brambilla V, Coruzzi P. Prognostic value of frontal QRS-T angle in patients undergoing myocardial revascularization or cardiac valve surgery. J Electrocardiol 2018; 51: 967-972.
13) Oehler A, Feldman T, Henrikson CA, Tereshchenko LG. QRS-T angle: a review. Ann Noninvasive Electrocardiol 2014; 19: 534-542.
14) Erdogan G, Yontar OC, Yenercag M, Gul S, Arslan U. Frontal QRS-T angle predicts syntax score in patients with non-ST elevation myocardial infarction. J Electrocardiol 2020; 61: 86-91.
15) Colluoglu T, Tanriverdi Z, Unal B, Ozcan EE, Dursun H, Kaya D. The role of baseline and post-procedural frontal plane QRS-T angles for cardiac risk assessment in patients with acute STEMI. Ann Noninvasive Electrocardiol 2018; 23: e12558.
16) Chua KC, Teodorescu C, Reinier K, Uy-Evanado A, Aro AL, Nair SG, Chugh H, Jui J, Chugh SS. Wide QRS-T Angle on the 12-Lead ECG as a Predictor of Sudden Death Beyond the LV Ejection Fraction. J Cardiovasc Electrophysiol 2016; 27: 833-839.

17) Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res 2020; 116: 1097-1100.
18) Kurisu S, Nitta K, Ikenaga H, Ishibashi K, Fukuda Y, Kihara Y. Frontal QRS-T angle and left ventricular diastolic function assessed by ECG-gated SPECT in the absence of significant perfusion abnormality. Heart Vessels 2020; 35: 1095-1101.
19) Haseeb S, Gul EE, Çinier G, Bazoukis G, Alvarez-Garcia J, Garcia-Zamora S, Lee S, Yeung C, Liu T, Tse G, Baranchuk A; International Society of Electrocardiology Young Community (ISE-YC). Value of electrocardiography in coronavirus disease 2019 (COVID-19). J Electrocardiol 2020; 62: 39-45.
20) Yenerçağ M, Arslan U, Doğduş M, Günal Ö, Öztürk ÇE, Aksan G, Erdoğan G, Gül S, Yontar OC, Şen A. Evaluation of electrocardiographic ventricular repolarization variables in patients with newly diagnosed COVID-19. J Electrocardiol 2020; 62: 5-9.