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Frontal QRS-T angle in COVID-19 patients with reduced left ventricular ejection fraction

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ABSTRACT

Aim: The frontal QRS-T angle has been recognized as an indicator of ventricular repolarization heterogeneity, and a large frontal QRS-T angle has shown promise as a reliable predictor of cardiac mortality and morbidity. This study aims to investigate the impact of baseline frontal QRS-T angles on the clinical severity of COVID-19 in patients with reduced left ventricular ejection fraction (LVEF).

Methods: In our study, we employed data from COVID-19 hospitalized patients admitted between January 1, 2020, and December 1, 2020. We included patients who underwent echocardiography during their hospitalization and those had a reduced LVEF (<40%). Patient admission to either the intensive care unit or general ward was determined in accordance with criteria established in the Ministry of Health guidelines during the initial phase. Subsequently, patients were categorized into two groups: the severe illness group and the mild/moderate illness group.

Results: Between the two groups, statistically significant differences were observed in terms of QT durations. In the severe illness group, the QTc interval was measured as 427 milliseconds, while in the mild/moderate illness group, it was recorded as 415 milliseconds ($p < 0.001$).

Additionally, the frontal QRS-T angle was determined to be 91.80±31.41 degrees in the severe illness group and 67.88±27.7 degrees in the mild/moderate illness group. Once again, a statistically significant difference was identified ($p < 0.001$).

Conclusion: Our study differs from previous studies in that our population included only patients with reducedLVEF . We determined that the frontal QRS-T angle may be a good indicator of disease severity in COVID-19 patients with reducedLVEF.

Kew words: COVID-19, heart failure, infection, QRS-T angle

INTRODUCTION

SARS-CoV-2, the etiological agent of COVID-19, has exhibited rapid global dissemination, leading to over 630 million confirmed cases and more than 6.6 million fatalities as of November 11, 20221.

Although COVID-19 can present as asymptomatic or with mild symptoms, it can give rise to severe complications, such as severe acute respiratory distress syndrome (SARS), renal or multiple organ failure, cardiac arrhythmia and even fatality. The prognosis is impacted by concomitant systemic diseases like diabetes, hypertension, chronic heart failure, and coronary artery diseases.[2,3] Besides cardiac comorbidities influencing the prognosis of COVID-19, the infection itself exerts detrimental impacts on the cardiovascular system. The myocardial repercussions of COVID-19 encompass acute coronary syndromes, myocarditis, decompensated heart failure, pulmonary embolisms, and arrhythmias. These effects manifest a broad spectrum of electrocardiogram (ECG) abnormalities.[4]

While COVID-19 carries a high mortality rate, the available predictive indicators for mortality are relatively scarce. Recently, investigations have focused on inflammatory and hematologic parameters, as well as imaging scoring systems, such as the Coronavirus Disease 2019 (COVID-19) Reporting and Data System (CO-RADS) classification, to assess disease severity and predict short-term mortality.[5,6,7]

The frontal QRS-T angle has been identified as an indicator of ventricular repolarization heterogeneity and a large frontal QRS-T angle is a good predictor of cardiac mortality and morbidity8. Change in the cardiac axis is one of the important electrocardiographic (ECG) finding in patients with COVID-19. In a study involving COVID-19 patients, mortality and mechanical ventilation requirement percentages were 67.8% and 66.1% in the frontal QRS-T angle >90° group, and 26.1% and 29.9% in the frontal QRS-T angle ≤90° group, respectively.[4,8] In a retrospective study comparing the data of polymerase chain reaction (PCR) positive and negative patients for COVID-19 in the study investigated the effect of the frontal QRS-T angle on disease severity. They found that frontal QRS-T increased significantly in severe illness patients.[9] When Mc Cullough et all. studied the ECGs of COVID-19 patients, they showed that 19.3% of the patients had an abnormal QRS axis10. The QT interval on surface ECG and the distance between the T wave peak and the endpoint can be used to assess myocardial repolarization.[11,12,13] The frontal QRS-T angle is simple to measure from the report portion of ECG devices.[14] Increased QRS-T angle indicates abnormal ventricular repolarization.[15] The available data regarding the association between the frontal QRS-T angle and the mortality rate as well as the clinical severity of COVID-19 patients is insufficient.

This study aims to determine the impact of baseline frontal QRS-T angles on the clinical severity of COVID-19 patients with reduced left ventricular ejection fraction.

METHODS

The study was carried out with the permission of Ethical Committe of Van Training and Researches Hospital Clinical Researches (Date:18.02.2021, Decision No: 2021-04). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. In our study, the data of COVID-19 hospitalized patients between 1 January 2020 and 1 December 2020 were used. Patients who underwent echocardiography during hospitalization and patients with reduced LVEF (<40%) were included ın the study. PCR negative patients, patients with bundle branch block in their ECGs, hemodialysis patients, patients under 20 years old, pregnant and lactating were excluded from the study. Besides, patients previously diagnosed with COVID-19 and followed up at home with medication were excluded. The patients were admitted to the intensive care unit or inward according to the criteria determined in the guidelines of the Ministry of Health during the first application. Patients were divided into two groups as severe illness group and the mild/moderate illness group.

In our center, routine ECGs are taken during the hospitalization of COVID-19 patients. Demographic and clinical characteristics, laboratory parameters, and length of hospital stay were obtained from the electronic medical records. Blood samples were analyzed for laboratory parameters such as urea, creatinine, sodium, potassium, glucose, D-dimer, hemoglobin, white blood cell, and C-reactive protein. Our study was approved by the local ethics committee.

Electrocardiography

At the time of initial hospitalization, the 12-lead ECGs of the patients were recorded (Tokyo, Japan, Nihon Kohden). The ECG calculations were performed in accordance with the guidelines. The automatic reports from the ECG machine included frontal QRS and T-wave axis. The frontal QRS-T angle on a 12-lead electrocardiogram was defined as: the QRS axis-T wave axis. In case the angle exceeded 180°, it was calculated by subtracting it from 36016,17

Statistical Analysis

Statistical Package for the Social Sciences 24.0 program was used. Descriptive statistics were given using frequency and mean ± standard deviation values. The relationship between numerical variables (heart rate, frontal QRS-T angle, QTc, QRS, CRP, WBC, lymphocites, D-Dimer, creatinine, BMI, Hbg, fasting glucose, sodium, potassium, urea, QT) evaluated with the independent sample t-test. Nominal/ordinal variables (sinus rhythm, diabetes mellitus, hypertension, smoking status, coronary artery desease, chronic obstructive pulmonary disease) were evaluated with two-way ANOVA and other numerical values were evaluated with ANOVA tests. p-values less than 0.05 and 0.001 were considered significant.

RESULTS

A total of 212 patients were included in the study. The mean age of patients was 65.32±11.53 years, and BMI was 28.77±3.62 kg/m2. It was seen that 51.4% of the mild/moderate illness group were male, 48.6% were female. While 48.5% of patients in severe illness group were female, 51.5% were male and 51.4% of patients in mild/moderate illness group were female, 48.6% were male. Both severe illness group (89.9%) and mild/moderate illness group (84.5%) sinus rhythms are mostly normal. The basic clinical and demographic characteristics, background, smoking history, laboratory values and ECG parameters were shown in **Table 1.**

There was no statistically difference in gender between the severe illness group and mild/moderate illness groups. When the severe illness group and mild/moderate illness groups were compared in terms of age, it was determined that the severe illness group was older. However, no significant differences in HT, DM, coronary artery disease, or smoking habit were found between the two groups. Chronic kidney disease, hemoglobin, WBC, lymphocyt, creatinine, urea, sodium, glucose, CRP, and D-dimer were different between the groups. **Table 2** also compares the ECG findings between the two groups. When the ECG findings were compared between the groups, the incidence of atrial fibrillation was found to be higher in the severe illness group than in the mild/moderate illness group, but this was not statistically significant (severe illness group=16/106 and mild/moderate illness group=11/109, p =0.235).

Mean heart rate was significiantly different between groups. The mean heart rate of the severe illness group was 88.27±18.64, the mean heart rate of the mild/moderate illness group was 80.85±14.11, and there was a significant difference (p< 0.001). Although the mean heart rate was higher in the severe illness group between the two groups, statistically significant results were found in terms of QT durations. QTc(427msec) in the severe illness group and QTc (415msec) in the mild/moderate illness group were calculated and there was significant statistical difference (p <0.001). The frontal QRS-T angle was 91.80±31.41 in the severe illness group and 67.88±27.7 in the mild/moderate illness group and significant statistical differece was found (p <0.000).

According to the results of the independent sample t test; angle [t(210)=-5.889, p=0.000], CRP [t(210)=-4.523, p=0.000], Hbg [t(210)=8.541, p=0.000], sodium [t(210)=-5.185, p=0.000] and urea [t(210)=-6.022, p=0.000] values are statistically significantly different between the groups (Table 2). According to independent sample t-test results, the mean of angle, CRP, sodium and urea were lower in mild/moderate illness group (angle=67.88±27.70; CRP=4.74±4.64; sodium=139.16±4.39; urea=42.18±12.23) than in severe illness group (angle=91.80±31.41; CRP=7.85±5.35; sodium=142.48±4.92; urea=52.88±13.62), while the mean Hbg was found to be higher in the mild/moderate illness group (13.98±1.66mg/dl) than the severe illness group (12.07±1.58mg/dl).

Two-way ANOVA was performed for the evaluation of nominal factors affecting the intergroup distribution, and ANOVA was applied for numerical factors. According to the two-way ANOVA test results, no nominal/ordinal factors affecting angle, Hbg, fasting blood sugar, sodium and urea were found (p>0.05). In addition, chronic kidney failure was found to affect the relationship between research groups and CRP [F(1)=73.05, p=0.007]. Accordingly, CRP values of patients in severe illness group ($\bar{x}$=3,44±3,78) with chronic kidney failure were considerably higher than those of patients in mild/moderate illness group ($\bar{x}$=11,68±3,26). According to ANOVA test results, no numerical factor affecting HBG, sodium and urea was encountered (p>0.05). In addition, it can be said that heart rate [F(1)=7.627, p=0.006] and fasting blood glucose level [F(1)=4.841, p=0.029] affect the intergroup distribution of the angle. In addition, it can be said that lymphocyte values [F(1)=19.392, p=0.000] and creatinine [F(1)=6.227, p=0.013] also affect CRP and intergroup distribution. Accordingly, the decrease in the angle of severe illness is affected by the low heart rate and fasting blood glucose. The distribution of intergroup distribution in CRP is affected by creatinine.

DISCUSSION

In the course of our investigation, it was discerned that there exists a noteworthy augmentation in the values of QTc duration and frontal QRS-T angle as the disease severity escalates. Our study distinguishes itself from previous research in that our study cohort exclusively comprised patients with reduced left ventricular ejection fraction. Our findings suggest that the frontal QRS-T angle could serve as a valuable indicator of disease severity in COVID-19 patients with compromised left ventricular function.

The frontal plane QRS-T (f(QRS-T)) angle, precisely defined as the angle between the vectors of ventricular depolarization (QRS axis) and repolarization (T axis), has been postulated as an innovative marker for assessing ventricular repolarization heterogeneity.[18]

The frontal QRS-T angle, which can be readily derived from the automated reporting section of electrocardiography (ECG) devices, is a highly valuable parameter. Its predictive significance has been demonstrated across various populations.[19,20]

Frontal QRS-T angle, as we are aware, serves as an indicator encompassing depolarization, repolarization, and heterogeneity and is easily quantifiable through ECG measurements. While observational studies have linked frontal QRS-T angle to mortality, the consensus on its association with both cardiac and all-cause mortality has not been consistently reinforced in numerous investigations.[21] In a groundbreaking study from 2003, spatial QRS angle emerged as a more robust predictor of mortality risk compared to traditional ECG parameters such as ST depression, T-wave inversion, and prolonged QT interval.[22]

It is unclear exactly how myocardial damage and arrhythmia caused due to COVID 19. Multiple organ failure is a hallmark of the advanced disease known as systemic inflammation.[23] Studies have shown that myocardial dysfunction in sepsis is caused by variables such as reduced contractility and altered cardiac conduction. Myocardial depression during sepsis is known to be correlated with the level of mediators and circulatory factors.[24]

In addition, it has been demonstrated that COVID-19 infection can induce autonomic dysfunction by activating the sympathetic nervous system and suppressing the parasympathetic system. This finding was highlighted in a study conducted by Del Rio R et al.[25]

Furthermore, a recent study comparing individuals who had recovered from COVID-19 to a healthy control group found that COVID-19 patients displayed a higher incidence of blunted heart rate response during exercise testing. This observation is believed to be a consequence of autonomic dysfunction.[26]

Previous research has concentrated on the spatial QRS-T angle, leaving the frontal QRS-T angle comparatively unexplored. The Finnish cohort research was the first large study to look into the relationship between the frontal QRS-T angle and sudden cardiac mortality. The study comprised 10.957 middle-aged people, and the risk of cardiac death was shown to be three times higher in the group with frontal QRS-T angles (>100°) than in the normal population.[27]

In examinations of COVID-19 patients, at least one ECG anomaly was observed. The major proposed mechanisms are cytokine storm, electrolyte problems, microthrombi, and coronary vasospasm.[28] Although practically all arrhythmias are encountered during COVID-19, sinus tachycardia is the most prevalent. Although both supraventricular and ventricular arrhythmias are common, ventricular arrhythmias are more fatal, as expected.[29] According to the literature, the rate of malignant arrhythmia in patients hospitalized with COVID-19 is as high as 16.7%; in patients hospitalized in the critical care unit, the rate can reach 44.4%.[30,31] Several ECG measurements have been proposed as potential indicators of malignant arrhythmias. Prolonged QTc and QTd due to ventricular repolarization abnormalities are risk factors that can enhance the likelihood of malignant arrhythmia.[32] In addition to these characteristics, we demonstrated that an increased frontal QRS-T angle could be an independent measure of disease severity. In our study, the difference in ECG (QTc, frontal QRS-T angle) between patients in the intensive care unit and those receiving the COVID-19 service suggests that the virus may impact ventricular depolarization and ventricular repolarization. This theory is supported by the fact that patients admitted to the COVID-19 service were similar to those admitted to the intensive care unit in terms of age and comorbidities. The frontal QRS-T angle, a simple ECG parameter, can aid in the management of COVID-19 patients and provide information on the severity of the disease throughout their follow-up. It can benefit in early care and decision-making until the findings of more advanced testing are available because it is readily available within minutes of contacting patients.

Study Limitations

Firstly, our study only included a small number of participants. We lacked information on coronary artery disease and hormone status that could trigger arrhythmia in our study participants. Investigations by echocardiogram were performed while the infection was active. Our study confined the number of examinations to a minimum in order to protect healthcare personnel from prolonged interaction.

CONCLUSION

The frontal QRS-T angle, which can be easily derived from ECG, was shown to be high in patients in severe illness group. The clinical severity of COVID-19 disease can be predicted using an increased

Table 1. Clinical Features of Patients According to Study Groups

Variables	Severe illness group (n=109)		Mild/moderate illness group (n=103)	
	n	%	n	%
Gender(male)	53	48.6	53	51.5
Atrial fibrilation	16	15.5	11	10.1
Hypertension	55	36.9	64	58.7
Diabetes mellitus	68	66.0	78	71.6
Chronic kidney disease	88	85.4	100	91.7
Smoking	67	65.0	70	64.2
Coronary artery disease	71	68.9	78	71.6
Chronic obstructive pulmonary disease	82	79.6	92	84.4

Table 2. Distribution of Patients According to Clinical Values

Variables	Severe illness group	Mild/ moderate illness group	p-value
Heart rate	88.27 ±18.64	80.85±14.11	0.001
F-QRS-T angle(°)	91.80 ±31.41	67.88±27.70	<0.001
QT (msec)	430.5 ±2.92	416.8±3.76	0.004
QTc (msec)	427.56±16.84	415.33±39.86	0.004
QRS (msec)	96.95±15.94	92.32±19.48	0.059
LVEF (%)	36.44±5.23	34.65±6.21	0.233
CRP (mg/L)	7.85±5.354	4.74±4.64	<0.001
WBC (10^3 /μl)	8.72±4.78	7.42±6.06	0.086
Lymphocytes (meq/L)	1055.33±796.56	1346.62±704.06	0.005
D-Dimer	2870.22±9659.31	1117.96±786.63	0.060
Creatinine (mg/dl)	1.17±0.81	0.86±0.353	0.001
Hgb(g/dl)	12.07±1.58	13.98±1.66	<0.001
Glucose (Fasting) (mg/dl)	112.28±31.15	101.27±30.83	0.010
Na+2 (mEq/L)	142.48±4.92	139.16±4.39	<0.001
K+ (mEq/L)	3.79±0.67	3.83±0.37	0.629
Urea (mg/dl)	52.88±12.23	42.18±13.62	<0.001
BMI	29.16±3.32	28.40±3.86	0.127

ETHICAL DECLARATIONS

Ethic Committee Approval: The study was carried out with the permission of Ethical Committe of Van Training and Researches Hospital Clinical Researches (Date:18.02.2021, Decision No: 2021-04).

Informed Consent: Written informed consent was obtained from the patients before the study.

Referee Evaluation Process: Externally peer-reviewed.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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