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Comparative study of frontal QRS-T angle and inflammatory parameters in obsessive compulsive disorder patients and healthy control group

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Abstract

It is argued that the average life expectancy for obsessive-compulsive disorder (OCD) decreases. However, data on the reasons for this are limited. This study compared sociodemographic characteristics, electrocardiogram (ECG) parameters, and laboratory values of 56 patients diagnosed with OCD with 60 healthy controls. We aimed to interpret the risk of cardiovascular disease in OCD through ECG parameters. OCD patients and the control group did not differ statistically in age or gender (p=0.689 and p=0.756, accordingly). Patient's with OCD have significantly longer corrected QT interval (QTc) (p=0.001). In comparison to the control group, OCD patients had statistically greater frontal QRS-T angle (fQRS-T) (p=0.044). The levels of platelet-to-lymphocyte ratio (PLR), pan immune inflammation value (PIV), and systemic immune inflammation index (SII) were elevated significantly in OCD patients (p=0.001, p=0.002, and p=0.009, respectively). The monocytes to high-density lipoprotein cholesterol (HDL-C) ratio (MHR) and atherogenic index of plasma (AIP) values of OCD patients were significantly greater than those of the control group (p<0.001 and p=0.006). Based on the Receiver Operating Characteristic (ROC) analysis, MHR had the highest area under curve (AUC) value (AUC=0.699, p<0.001, cut-off=0.0097). It was determined that a 0.0097 increase in MHR value could be used in diagnosing OCD with 66% sensitivity and 71% specificity. According to the results of our study, cardiovascular mortality can be predicted by measuring fQRS-T in the electrocardiogram or AIP and MHR values in laboratory findings in OCD patients, and treatments and recommendations can be made in this regard. Calculating MHR and fQRS-T can also be used in routine practice because it is inexpensive and easy to apply. It seems possible that clinicians can reduce mortality and morbidity in this patient group by examining these parameters more in routine practice.

Keywords: Obsessive-compulsive disorder, frontal QRS-T angle, monosit HDL ratio, atherogenic index of plasma

Introduction

Obsessive-compulsive disorder (OCD) consists of disturbing obsessions, repetitive compulsions that relieve anxiety and restlessness resulting from these obsessions, and avoidance of environments and situations that trigger obsessions [1]. The average frequency of OCD in the general public is 1.2%, and the lifetime prevalence of OCD is accepted as 2.3% [2].

It is argued that the average life expectancy of people with OCD declines. However, data on the reasons for this are limited [3]. Cardiovascular diseases are responsible for 31% of all deaths, and it is thought that cardiovascular diseases are more common than severe mental diseases [4]. However, OCD has rarely been studied separately from other psychiatric disorders. The most extensive study on this subject in OCD patients was done by Isomura et al. in 2018 in the Swedish population. Isomura et al. reported that the prevalence of cardiovascular disease increased by 44% in OCD patients [5].

Frontal QRS-T angle (fQRS-T) represents heterogeneity of myocardial depolarization and repolarization. There is a distinction between the QRS axis showing myocardial depolarization and the T axis showing myocardial repolarization, which is called fQRS-T. The electrocardiogram (ECG) is a simple tool for calculating this novel marker. Information in the literature implies that fQRS-T may be an indicator of cardiovascular diseases [6].

As functionality declines over time, treatment compliance changes, and treatments are used, it is vital to determine the risk of cardiovascular ailments in OCD sufferers. ECG is a fast,

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inexpensive, easily accessible, and quickly evaluated test. In the current study, we compared the sociodemographic features, ECG data, and laboratory values of 56 subjects we followed with the diagnosis of OCD with 60 healthy volunteers. We aimed to interpret the risk of cardiovascular disease in OCD through ECG parameters.

Materials and Methods

Study Design

Research methodology approval was provided by the Academic Ethical Review Committee of the University of Adıyaman (Approval date: 2021-12-14; IRB Number: 2021/10-22). The research was carried out with the signed consent of all subjects. The Declaration of Helsinki was followed during the process of the research. The research is cross-sectional and descriptive in nature.

Study Group

This study included 56 OCD patients diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [7] and 60 healthy controls without any psychiatric or organic disease. The inclusion criteria for OCD and healthy control groups were i) not having hypertension, coronary artery disease, valve disease, and arrhythmias, ii) be above age 18 and under age 65, and iii) not having severe neurological disorders (dementia, cerebrovascular disease, etc.) and alcohol or substance use disorder. Age, gender, smoking status, hemogram, biochemistry, systolic and diastolic blood pressures, and ECG parameters of the participants were used. Participants' BMI was calculated by dividing their weight by their height squared.

Electrocardiogram Examination

All patients were given a 12-lead ECG (Nihon Kohden, Tokyo, Japan) featuring a 10mm/mV amplitude, 25mm/s rate, and 0.16-100 Hz filtering range while lying supine. The measurements of the QRS and QT intervals were generated by software. The duration after the onset of a Q wave and the conclusion of a S wave is known as the QRS duration. The QT interval is the space between the commencement of the QRS wave and the conclusion of the T wave. The heart rhythm affects how long the QT interval lasts (as the heart rate rises, the QT interval decreases, while as the rate falls, the QT interval lengthens). Consequently, it must be adjusted according to the heart rate. The corrected QT interval (QTc) is predicted using a baseline heart rate of 60 beats per minute. The QT interval is modified for heart rate via the Bazett method. The QRS and T axes were already included in the ECG device's output. The exact distance between the QRS axis and the T axis was used in the report to determine the fQRS-T angle. 360 degrees are subtracted from the difference to determine angles higher than 180 degrees.

Laboratory Examination

A venous blood sample was collected on admittance to hospital. An Architect c8000 Chemistry System (Abbott Diagnostics, USA) was used to measure low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol (total-C), and fasting triglyceride concentrations. An electronic hematology testing device CELL-DYN Ruby (Abbott Diagnostics, Abbott Park, IL, USA) was used to measure white blood cells (WBC), including neutrophils and lymphocytes. The hemoglobin, albumin, and platelet counts were also determined. A neutrophil-to-lymphocyte ratio (NLR) was computed by dividing the quantity of neutrophils by the quantity of lymphocytes, a monocyte-to-lymphocyte ratio (MLR) was calculated by dividing the count of monocytes by the count of lymphocytes, and a platelet-to-lymphocyte ratio (PLR) is calculated by dividing the count of platelets by the count of lymphocytes. The neutrophils to albumin ratio (NAR) and the monocytes to HDL-C ratio (MHR) were also assessed. The atherogenic index of plasma (AIP) is calculated as a logarithm (fasting triglyceride/HDL-C). Based on the exact measurements of total blood concentrations, the pan immune inflammation value (PIV) was calculated as follows: PIV =[neutrophils (10^6/mm^3)× platelets (10^3/mm^3)× monocytes (10^3/mm^3)]/lymphocytes (10^3/mm^3). In order to calculate the systemic immune inflammation index (SII), the following formula was used: SII=[neutrophils (10^6/mm^3)× platelets (10^3/mm^3)]/lymphocytes (10^3/mm^3).

Statistical Analysis

Evaluation of data was conducted utilizing SPSS software 26.0 (SPSS Inc., Chicago, IL, U.S.A.). Means and standard deviations were utilized to represent numerical variables, and percentages to represent qualitative variables. An analysis of data patterns was done using the Kolmogorov-Smirnov test. When comparing numerical variables, independent sample t-tests were applied, while Mann-Whitney U tests were employed for discontinuous numerical variables. Chi-square tests were conducted to compare qualitative variables within the study group. Diagnostic sensitivity and specificity were examined using Receiver Operating Characteristic (ROC) methods.

Results

Sociodemografic parameters

OCD patients and the control group did not differ statistically in age or gender ($p=0.689$ and $p=0.756$, accordingly). Healthy controls and OCD patients had similar BMIs ($p=0.602$). In OCD patients and healthy controls, smoking status was not significantly different ($p=0.467$).

ECG-related parameters

In comparison to healthy controls, OCD patients had no difference in heart rate, QT, and QRS. Patient's with OCD have significantly longer QTc ($p=0.001$). In comparison to the control group, OCD patients had statistically greater fQRS-T ($p=0.044$).

Laboratory parameters

Both groups had similar hemoglobin values. OCD patients had low albumin levels ($p=0.011$). WBC, neutrophils, lymphocytes, and eosinophils did not differ between the groups. The basophil count in OCD patients was significantly lower ($p<0.001$). There was a statistically significant rise in monocyte count in OCD patients ($p=0.094$). There was a marked increase in platelet count in the OCD group versus the control group ($p<0.001$).

OCD patients had significantly higher total and LDL cholesterol

(p=0.002 and p<0.001, respectively). Patients with OCD had significantly reduced HDL-C levels (p<0.001).

Table 1. Comparison of Sociodemographic Features and Electrocardiographic Parameters of Obsessive Compulsive Disorder Patients and Healthy Controls

	OCD(n=56)	HC(n=60)	p
Age	36.96±10.57	35.78±9.5	0.689[1]
Gender			0.756[2]
Female	34 (60.7)	38 (63.3)	
Male	22 (39.3)	22 (36.7)	
Smoking	23 (41)	21 (35)	0.467[2]
BMI, kg/m²	26.87±5.49	26.4±5.1	0.602[1]
Systolic blood pressure mmHg	119.4±10.7	116.4±15.3	0.551[1]
Diastolic blood pressure mmHg	77.4±6.8	73.6±8.6	0.411[1]
Heart rate, bpm	83.11±16.32	77.75±12.18	0.065[3]
QRS, msec	86.04±7.58	88.83±7.26	0.328[1]
QT, msec	371.43±34.08	366.43±26.7	0.526[3]
QTc, msec	433.59±30.71	403.3±27.04	0.001[1]
fQRS-T	26.79±21.08	19.85±15.31	0.044[3]

OCD, obsessive compulsive disorder; HC, healthy control; BMI, body mass index; fQRS-T, frontal QRS-T angle; QTc, corrected QT interval
[1]Independent t test was used. [2]Chi-square test was used. [3]Mann-Whitney U test was used. p<0.05 was accepted as statistically significant

Table 2. Comparison of Laboratory Parameters of Obsessive Compulsive Disorder Patients and Healthy Controls

	OCD (n=56)	HC (n=60)	p
Hemoglobin, mg/dL	13.66±2.22	14.51±2.11	0.038[1]
Albumin, mg/dL	4.11±0.38	4.3±0.28	0.011[2]
WBC, 10³/µL	7.76±1.77	8.15±2.11	0.292[1]
Neutrophil, 10⁶/µL	5.08±3.53	4.86±1.67	0.976[2]
Lymphocyte, 10³/µL	2.52±1.54	2.51±0.77	0.192[2]
Monocyte, 10³/µL	0.60±0.21	0.53±0.20	0.094[1]
Eosinophil, 10³/µL	0.15±0.12	0.13±0.10	0.263[2]
Basophil, 10³/µL	0.04±0.04	0.09±0.04	<0.001[2]
Platelet, 10³/µL	291.83±60.98	242.67±44.31	<0.001[2]
Total-C, mg/dL	191.96±46.07	166.83±38.79	0.002[1]
LDL-C, mg/dL	109.82±37.08	75.26±28.72	<0.001[2]
HDL-C, mg/dL	49.93±14.44	65.87±14.56	<0.001[1]
Fasting Triglyceride, mg/dL	172.85±165.97	128.63±108.89	0.157[2]

OCD, obsessive compulsive disorder; HC, healthy control; WBC, white blood cell; Total-C, total cholesterol; LDL-C, low-density cholesterol; HDL-C, high-density cholesterol
[1]Independent t test was used. [2]Mann-Whitney U test was used. p<0.05 was accepted as statistically significant

Inflammatory Parameters

The levels of PLR, PIV, and SII were elevated significantly in OCD patients (p=0.001, p=0.002, and p=0.009). No differences were observed between the groups for NLR, MLR, and NAR. The MHR and AIP values of OCD patients were significantly greater than those of the control group (p<0.001 and p=0.006).

Based on the ROC analysis, MHR had the highest area under curve (AUC) value (AUC=0.699, p<0.001, cut-off=0.0097). It was determined that a 0.0097 increase in MHR value could be used in diagnosing OCD with 66% sensitivity and 71% specificity.

Table 3. Comparison of Inflamatory Parameters of Obsessive Compulsive Disorder Patients and Healthy Controls

	OCD (n=56)	HC (n=60)	p
NLR	2.25±1.52	2.12±1.06	0.328[2]
MLR	0.27±0.12	0.23±0.13	0.051[2]
PLR	131.96±49.01	107.08±46.18	0.001[2]
PIV	394.23±311.23	275.48±198.8	0.002[2]
SII	646.28±399.96	523.51±313.14	0.009[2]
MHR	0.010±0.007	0.008±0.003	<0.001[1]
NAR	1.24±0.8	1.13±0.4	0.473[2]
AIP	0.42±0.41	0.2±0.31	0.006[2]

OCD, obsessive compulsive disorder; HC, healthy control; NLR; neutrophil lymphocyte ratio; MLR, monocyte lymphocyte ratio; PLR, platelet lymphocyte ratio; PIV, pan immune inflammation value; SII, systemic immune inflammation index; MHR, monocyte HDL-C ratio; NAR, neutrophil albumin ratio; AIP, atherogenic index of plasma
1Independent t test was used. 2Mann-Whitney U test was used. p <0.05 was accepted as statistically significant.

Table 4. Evaluation of Inflammatory Parameters According to ROC Analysis

	AUC	p	%95 CI	
			Lower Bound	Upper Bound
PLR	0.687	0.001	0.588	0.786
MHR	0.699	<0.001	0.600	0.798
PIV	0.658	0.003	0.557	0.759
SII	0.639	0.010	0.535	0.743
AIP	0.649	0.006	0.549	0.749
fQRS-T	0.582	0.132	0.476	0.687

ROC, receiver operating characteristic; AUC, area under curve; CI, confidence interval; PLR, platelet lymphocyte ratio; MHR, monocyte HDL-C ratio; PIV, pan immune inflammation value; SII, systemic immune inflammation index; NAR, neutrophil albumin ratio; AIP, atherogenic index of plasma; fQRS-T: frontal QRS-T angle
ROC curve analyses was used. p <0.05 was accepted as statistically significant

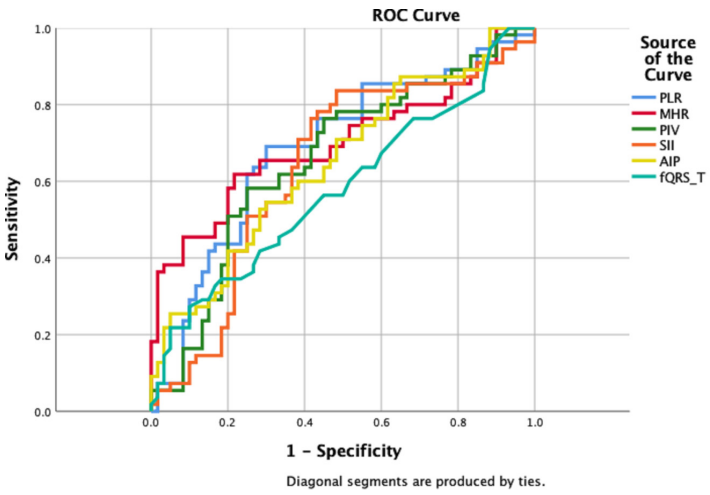

Figure 1. ROC Curve of Inflammation Parameters

Discussion

According to our study, people with OCD had a greater fQRS-T angle on their electrocardiogram than healthy people. In addition, our study found QTc to be significantly longer in OCD patients.

Wide fQRS-T was strongly associated with cardiovascular mortality in a large-scale meta-analysis conducted in 2014 [8]. Severe mental diseases have been linked to cardiovascular death in previous studies [9]. In 2020, Isomura et al. examined cardiovascular morbidity in OCD patients for the first time and observed that cardiovascular morbidity increased by 25% in OCD patients. They found that this increase was mainly associated with a 48% increase in venous thromboembolism and a 37% increase in heart failure. [10].

It is known that there are changes in autonomic nervous system functions in anxiety disorders [11,12]. An increase in sympathetic branch activity has been reported primarily in these diseases [13]. Moreover, OCD patients have been reported to exhibit increased sympathetic and decreased parasympathetic activity [14,15]. In a study conducted with OCD patients with heart rate variability, it was determined that the mean heart rate was higher in OCD patients, and it was thought that the autonomic nervous system sympathetic response was higher in OCD patients [16].

Neurotic disorders provide perhaps the strongest evidence suggesting interoceptive signaling is involved in inflammation. Human meta-analyses reveal that stress is an essential factor associated with persistent inflammation, particularly in early life. The immune function and the brain interact bidirectionally in this stress sensitivity [17].

Inflammation takes an increasingly significant part in the development of many prevalent mental illnesses. Interoceptive mechanisms have a crucial function in transmitting immune status to the brain. Activation of the immune system in the body begins with a response system against injury and pathogens and is distributed throughout the body. The response begins with various patterns. Immune mediators and inflammatory molecules, primarily cytokines, are secreted during this response. Additionally, interoceptive pathways transmit messages between the immune system and neurons, triggering the brain's emotional, neurovegetative, motivational, and cognitive responses [18-20].

As a neurotic disorder, OCD is associated with increased inflammation as shown by the significantly higher PIV and SII levels in our study. Evidence from studies on the effect of inflammation on atherogenesis has reached broad levels. A recent clinical study has shown that monoclonal antibodies administered specifically targeting interleukin-beta without affecting plasma LDL-C, lipids, or lipoproteins reduce cardiovascular events [21,22].

MHR is a cost-effective, simple, and cheaper method than other inflammation markers and is an essential index in demonstrating cardiovascular events and atherosclerosis development. It is an index that is easy to use in daily practice due to its correlation with common inflammation indicators like C-reactive protein (CRP). The presence of a high MHR value was related to worse outcomes, along with increased disease severity and progression [23]. Previous studies have also linked AIP value to cardiovascular mortality. According to a prior study, it has a higher potential as a cardiovascular indicator in schizophrenia [24].

In our study, the MHR and AIP values were considerably greater in the OCD group in comparison to the control group, indicating that the inflammatory process significantly increased in OCD, which may be associated with cardiovascular mortality by accelerating atherosclerosis.

Since our study was not performed in a large cohort, performing it in a larger OCD population will make the results more meaningful. The exclusion of drugs used by OCD patients in our study limited the study as it may affect the QT interval and QTc distances, and ventricular repolarization on the electrocardiogram. The lack of blood electrolyte levels, glucose, and thyroid hormone levels in the patients is one of the limitations of our study. Due to the fact that our study is the first to investigate the relationship between OCD and fQRS-T, it was not possible to compare it to other studies. Nevertheless, our study is valuable for the literature as it brings a new light to the literature.

Conclusion

According to the results of our study, cardiovascular mortality can be predicted by measuring fQRS-T in the electrocardiogram or AIP and MHR values in laboratory findings in OCD patients, and treatments and recommendations can be made in this regard. Calculating MHR and fQRS-T can also be used in routine practice because it is inexpensive and easy to apply. It seems possible that clinicians can reduce mortality and morbidity in this patient group by examining these parameters more in routine practice.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical approval
Research methodology approval was provided by the Academic Ethical Review Committee of the University of Adıyaman (Approval date: 2021-12-14; IRB Number: 2021 / 10-22).

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