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Comparison of frontal QRS-T angle and inflammatory parameters in patients with major depressive disorder and healthy controls

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Summary

Background: *Major depressive disorder (MDD) is known as risk factor for developing cardiovascular disease. This study aimed to evaluate the risk of cardiovascular disease in drug-naive patients diagnosed with MDD by evaluating frontal QRS-T angle (fQRS-T) and laboratory parameters.*

Subjects and methods: *Fifty-nine MDD patients (28 females, 31 males) and 61 healthy controls (HC) (39 females, 22 males) were included in the study. Electrocardiography (ECG), lipid parameters, hemogram, and biochemistry values of the participants were taken. Hamilton Depression Rating Scale (HDRS) was used to determine the severity of MDD. Monocyte lymphocyte ratio (MLR), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), monocyte high density cholesterol (HDL-C) ratio (MHR), and C-reactive protein albumin ratio (CAR) were calculated.*

Results: *The mean age was 34.54±7.10 years in the MDD group and 32.80±6.78 years in the HC group. The fQRS-T value ($p<0.001$) was significantly higher in the MDD group than in the HC group. MLR ($p<0.001$), NLR ($p<0.001$), and PLR values ($p<0.001$) were significantly higher in the MDD group than in the HC group. A significant positive correlation was found between MLR, NLR, PLR, HDRS and fQRS-T angle in the MDD group. According to the linear regression analysis for fQRS-T, NLR positively and significantly predict fQRS-T [$F=34.700$, $p<0.001$, adjusted R square=0.635].*

Conclusion: *This current study is the first to show that there is a significant positive relationship between NLR, MLR, PLR levels and depression severity and fQRS-T angle in patients diagnosed with MDD.*

Keywords: *Major depressive disorder, cardiovascular disease, electrocardiogram, inflammation*

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INTRODUCTION

Major depressive disorder (MDD) is a psychiatric disorder that primarily affects women and may result in disability. It involves a depressed mood or loss of pleasure or interest in activities for long periods and it can cause difficulties in all aspects of life, including in the community and at home, work, and school. A complex interplay of biological, psychological, and social factors leads to MDD (Astafeva et al., 2023). In the world, 280 million people suffer with MDD. More than 700,000 people die due to suicide every year. The fourth most common cause of mortality for people aged 15 to 29 is suicide (https://www.who.int/news-room/fact-sheets/detail/depression). Physical health is intimately tied to and impacts depression. Many of the factors that influence depression are also known risk factors for diseases such as cardiovascular disease (CVD), cancer, diabetes, and respiratory diseases. As a result of the challenges involved in controlling their illness, those who have certain conditions may also develop MDD (Gold et al., 2020).

The link between CVDs and depression has been known for a long time. MDD is known as risk factor for developing CVD, which is as important and is independent of classic risk factors, such as hypertension, diabetes mellitus, and smoking. Studies indicate that MDD is more common in those who have experienced a major cardiac event, as many as 40% of patients fit the criteria for MDD. MDD was associated with an overall relative risk of 1.64 for developing CVD, according to a meta-analysis of 11 trials (Katon et al., 2004). The likelihood of having CVD is correlated with the severity of depression (Ren, 2022). Various mechanisms, including hypothalamic-pituitary-adrenal axis dysfunction, autonomic disorders, metabolic derangements, endothelial damage, hematological changes, behavioral factors, childhood traumas, genetic factors, and inflammation, play a role in the relationship between cardiovascular disease risk

and depression (Ozturk et al., 2023). Individuals with MDD may also have dysregulation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system as a result of psychological stress. The development of hypertension, coronary vasoconstriction, platelet activation, heart rate variability, left ventricular hypertrophy, endothelial dysfunction, and the release of pro-inflammatory cytokines are among the detrimental downstream effects that follow. Furthermore, the patients diagnosed with MDD have higher rates of detection for cardiac risk factors, including smoking, diabetes, alcoholism, dyslipidemia, and sedentary lifestyles. An increased risk of myocardial infarction and ventricular arrhythmias could result from this (Dhar & Barton, 2016).

Frontal QRS-T angle (fQRS-T) is a non-invasive and simple ECG parameter that can be simply computed from electrocardiography (ECG) without requiring any special software. The fQRS-T is the definite angle diffraction between the QRS and T axes. This ECG parameter is quite recent and provides valuable insight into the process of myocardial repolarization (Dilaveris et al. 2001). In a variety of populations, researchers have shown that fQRS-T can predict impending cardiovascular events, this parameter has also been connected to arrhythmias and sudden death (Oehler et al,. 2014). Yilmaz and Yilmaz compared the fQRS-T angles of patients diagnosed with MDD and healthy controls and found that this value was significantly higher in the patient group (Yilmaz & Yilmaz, 2023). However, in that study, the relationship between inflammation parameters, whose role in CVD has been frequently studied, and ECG parameters was not investigated. Systemic inflammation has been emphasized in the literature as a significant factor in the onset, course, and prognosis of atherosclerosis in recent years. Lymphocyte, C-reactive protein, cholesterol and albumin related parameters have been frequently investigated for this purpose.

To the best of our knowledge, there is no information on the relationship of fQRS-T angle, inflammation parameters, and MDD. This study aimed to evaluate the risk of cardiovascular disease in drug-naive patients diagnosed with MDD by evaluating fQRS-T angle and laboratory parameters.

SUBJECTS AND METHODS

The present study have a cross-sectional nature. This study was carried out in Adıyaman Training and Research Hospital in Turkey. The ethics committee of Adıyaman University gave its clearance to the study (Decision Date: 16/11/2021 and Decision Number: 2021/09-03). The Declaration of Helsinki was followed in conducting the study.

Fifty-nine patients diagnosed with MDD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) were included in the study (American Psychiatric Association, 2013). Those who were not between the ages of 18 and 65, those with known cardiac disease, endocrinology disease, and other psychiatric disorders were excluded from the study. All patients diagnosed with MDD were drug-naive. Sixty-one healthy control (HC) subjects without a known disease were included in the study. The HC group was selected from the people who came to get a driver's license, a job entrance examination, or a healthy report. Participants of HC group were not using any psychotropic, antiarrhythmic drugs such as calcium channel blockers or beta blockers. Some sociodemographic (age, gender, and smoking status) and clinical (complete blood count, biochemistry, and ECG parameters) features of the participants were recorded.

The 17-item Hamilton Depression Rating Scale (HDRS), which was developed in late 1950s has been the most frequently used observer-rated measure of depression. The HDRS evaluates depression severity through items on: 1) depressed mood, 2) guilt, 3) suicidal thought or action, 4) insomnia initial, 5) insomnia middle, 6) insomnia late, 7) work and interests (assessing pleasure and functioning), 8) motor retardation, 9) motor agitation, 10) psychic anxiety, 11) somatic anxiety, 12) appetite, 13) tiredness, 14) sexual interest, 15) hypochondriasis, 16) weight loss, 17) insight. Among these 17 items, 9 items are scored on a 5-point scale (0–4) and 8 items on 3-point scale (0–2) with higher scores indicating greater depressive severity for all items. In keeping with current practice, the total item score was used to quantify the severity of depression (Hamilton, 1960). The Turkish validity and reliability study of HDRS was carried out by Akdemir et al. (Akdemir et al., 1996).

Every participant had their 12-lead ECG (Nihon Kohden, Tokyo, Japan) monitored. The settings for the QRS and QT intervals were generated methodically. QRS duration was calculated from the beginning of the Q wave to the end of the S wave. The time between the start of the QRS and the conclusion of the T wave was referred to as the QT interval. The QT interval varies according to heart rate; it shortens when heart rate rises and lengthens when heart rate falls. As a result, it must be changed in accordance with heart rate. The QT interval at a constant heart rate of 60 is represented by the corrected QT interval (QTc). It was easy to find the QRS and T axes in the ECG machine's documentation. The actual difference between the QRS and T axes was used to calculate the fQRS-T

after they were verified by the report. ECG examination was performed by an 9-year-experienced cardiologist.

The volunteers gave a venous blood sample when they were admitted to the hospital. To quantify white blood cells (WBC), including neutrophils and lymphocytes, CELL-DYN Ruby (Abbott Diagnostics, Abbott Park, IL, USA) was used the computerized hematology testing instrument. Lymphocyte-related ratios such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR); hemoglobin, low density cholesterol (LDL-C), high density cholesterol (HDL-C), monocyte HDL-C ratio (MHR), and C-reactive protein the albumin ratio (CAR) were also measured.

Windows SPSS 22.0 (Statistical Package for the Social Sciences Inc.) was used for the statistical analysis. Continuous variables and descriptive statistics are presented as mean±standard deviation, while categorical variables are presented as frequency and percentage. The categorical data were analyzed using the chi-square test. The Kolmogorov-Smirnov test was used to determine whether a normal distribution was appropriate. Mann-Whitney U test was used to make comparisons between two groups to determine significant differences between groups. ROC curve analysis was used to measure the diagnostic value of lymphocyte-related parameters and fQRS-T angle. Spearman correlation analysis was performed to the

Table 1. Comparison of Sociodemographic and ECG Parameters of Patients Diagnosed with MDD and HC

Variables		MDD (n=59)	HC (n=61)	p
Age (years)		34.54±7.10	32.80±6.78	0.173
Gender (n/%)	**Female**	28	39	0.069
	Male	31	22	
Smokers (n/%)		22 (36.1%)	29 (49.2%)	0.147
Heart rate, bpm		82.90±14.37	77.41±12.94	0.030*
QRS, msec		89.80±8.95	87.87±8.35	0.225
QT, msec		365.66±28.74	368.92±28.84	0.537
QTc, msec		414.53±29.92	406.56±29.96	0.148
fQRS-T (o)		48.05±18.84	21.21±16.59	<0.001*
HDRS		36.50±11.14	–	–

*p<0.05; Independent t test and Chi-square test were used; MDD: Major depressive disorder, HC: Healthy controls, ECG: Electrocardiography, QTc: Corrected QT interval, fQRS-T: Frontal QRS-T angle, HDRS: Hamilton depression rating scale

Table 2. Comparison of Complete Blood Count Parameters of Patients Diagnosed with MDD and HC

Variables	MDD (n=59)	HC (n=61)	p
Hemoglobin, mg/dL	14.87±1.88	14.40±2.24	0.218
WBC, 103**/µL**	8.11±2.01	8.12±2.12	0.981
Neutrophil, 106**/µL**	5.56±1.62	4.84±1.62	0.017*
Lymphocyte, 103**/µL**	1.73±0.81	2.50±1.12	<0.001*
Monocyte, 103**/µL**	0.56±0.23	0.55±0.20	0.749
Eosinophil, 103**/µL**	0.13±0.11	0.16±0.14	0.201
Basophil, 103**/µL**	0.07±0.04	0.09±0.05	0.125
Platelet, 103**/µL**	252.11±43.74	242.04±48.39	0.235
MLR	0.37±0.22	0.24±0.13	<0.001*
NLR	3.75±1.47	2.23±1.18	<0.001*
PLR	174.02±78.06	110.45±47.09	<0.001*

*p<0.05; Independent t test was used; Abbreviations=MDD: Major depressive disorder, HC: Healthy controls, WBC: White blood cell, MLR: Monocyte lymphocyte ratio, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio

Table 3. Comparison of Biochemical Parameters of Patients Diagnosed with MDD and HC

Variables	MDD (n=59)	HC (n=61)	p
Albumin, mg/dL	3.94±0.23	4.28±0.47	<0.001*
CRP, mg/dL	0.29±0.11	0.24±0.23	0.184
Total cholesterol, mg/dL	176.17±44.26	170.30±39.39	0.444
LDL-C, mg/dL	82.03±29.11	76.65±28.81	0.318
HDL-C, mg/dL	59.15±15.51	67.61±18.06	0.007*
Triglyceride, mg/dL	170.53±146.80	127.51±11.59	0.073
MHR	0.010±0.005	0.008±0.003	0.082
CAR	0.074±0.030	0.059±0.069	0.136

*p<0.05; Independent t test was used; Abbreviations=MDD: Major depressive disorder, HC: Healthy controls, CRP: C-reactive protein, LDL: Low density cholesterol, HDL: High density cholesterol, MHR: Monocyte HDL-C ratio, CAR:C-reactive protein albumin ratio

patient group. Linear regression analysis was performed to assess the impact of lymphocyte-related parameters on the fQRS-T angle. Binary logistic regression analysis was used in group prediction. A value of less than 0.05 (p value) was considered statistically significant.

RESULTS

There were 31 males (52.54%) and 28 females (47.46%) in MDD group, 22 males (36.06%) and 39 females (63.94%) in the HC group. The mean age was 34.54±7.10 years in the MDD group and 32.80±6.78 years in the HC group. There was no significant difference between the MDD and HC groups in terms of age (p=0.173), gender (p=0.069), and smoking status (p=0.147). While the QRS (p=0.225), QT (p=0.537), QTc values (p=0.148) of the MDD and HC groups were similar, the fQRS-T value (p<0.001) was significantly higher in the MDD group than in the HC group (Table 1).

Complete blood count (CBC) and other laboratory parameters of MDD and HC groups were compared (Table 2 and Table 3). MLR (p<0.001), NLR (p<0.001), and PLR values (p<0.001) were significantly higher in the MDD group than in the HC group. The lymphocyte count was significantly higher in the HC group than in the MDD group (p<0.001). Albumin value was significantly higher in the HC group than in the MDD group (p<0.001).

Correlation of various parameters with fQRS-T angle by controlling for the age effect was shown in Table 4. A significant negative correlation was found between lymphocyte count and fQRS-T angle in the MDD group. Also, a significant positive correlation was found between MLR, NLR, PLR, HDRS and fQRS-T angle in the MDD group.

Table 4. Correlation analyses of fQRS-T angle and laboratory parameters in patients with MDD controlling for the effect of age

Variables	fQRS-T Angle (r, p)
MLR	0.608, <0.001*
NLR	0.789, <0.001*
PLR	0.672, <0.001*
Lymphocyte	-0.590, <0.001*
HDRS	0.495, <0.001*

*p<0.05; Pearson correlation analyses was used; Abbreviations= fQRS-T: Frontal QRS-T angle, MDD: Major depressive disorder, MLR: Monocyte lymphocyte ratio, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, HDRS: Hamilton depression rating scale

In the MDD group, the relationship between HDRS score and lymphocyte-related parameters was examined by controlling the effect of age. A significant positive correlation was found between MLR (r=0.583, p<0.001), NLR (r=0.664, p<0.001), PLR (r=0.759, p<0.001) and HDRS.

Linear regression analysis was applied to evaluate the effect of MLR, NLR, PLR on fQRS-T. Accordingly, the regression model was significant since p<0.001 for ANOVA test. According to the linear regression analysis for fQRS-T, NLR positively and significantly predict fQRS-T [F=34.700, p<0.001, adjusted R square=0.635] (Table 5).

According to the binary logistic regression analysis, the sensitivity of fQRS-T angle (p<0.001) related to the diagnosis of MDD was 76.3 percent and the specificity

Table 5. Linear regression analyses of fQRS-T angle in MDD group

	Unstandardized Coefficients		Standardized Coefficients	t	p	95,0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	9.216	4.128		2.232	0.030*	0.942	17.489
MLR	14.278	9.462	0.167	1.509	0.137	-4.683	33.240
NLR	8.284	1.655	0.647	5.004	<0.001*	4.967	11.602
PLR	0.013	0.033	0.055	0.401	0.690	-0.053	0.080

*p<0.05; Linear regression analyses was used; Abbreviations= fQRS-T: Frontal QRS-T angle, MDD: Major depressive disorder, MLR: Monocyte lymphocyte ratio, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio

was 80.3 percent (Exp(B)=1.080 [95%CI for Exp(B) = 1.052-1.110], Constant p<0.001; -2 Log likelihood = 114.638; Cox & Snell R^2= 0.350; Nagelkerke R^2=0.467).

According to the binary logistic regression analysis, the sensitivity of NLR (p<0.001) related to the diagnosis of MDD was 72.9 percent and the specificity was 82.0 percent (Exp(B)=2.265 [95%CI for Exp(B) = 1.637-3.132], Constant p<0.001; -2 Log likelihood = 133.110; Cox & Snell R^2= 0.242; Nagelkerke R^2=0.322).

ROC curve analysis performed on the basis of patients diagnosed with MDD and HCs. Area under the curve was 0.858 for fQRS-T (p<0.001), 0.718 for MLR (p<0.001), 0.784 for NLR (p<0.001), and 0.776 for PLR (p<0.001) (Figure 1).

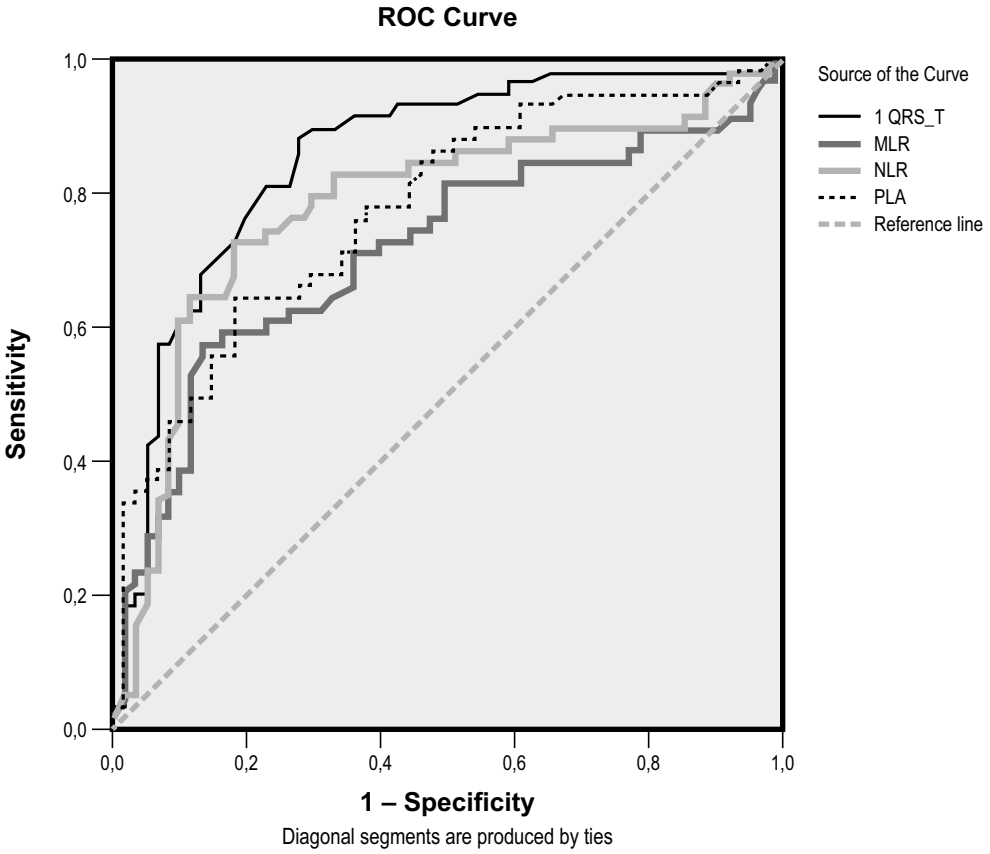

Figure 1. ROC Curve Analysis of fQRS-T Angle and Lymphocyte-Related Parameters

Notes: fQRS-T: Frontal QRS-T angle, MLR: Monocyte lymphocyte ratio, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio

DISCUSSION

This study compares the ECG and laboratory parameters of drug-naïve MDD and HC groups. It has been demonstrated that the fQRS-T angle, MLR, NLR, and PLR of the MDD group were significantly higher than the HC group. A significant positive correlation was found between MLR, NLR, PLR, HDRS and fQRS-T angle in the MDD group.

Future cardiovascular mortality can be predicted by abnormalities in ventricular depolarization, particularly changes during the vulnerable repolarization phase in particular. Many studies have demonstrated the ability to predict cardiac mortality based on the spatial QRS-T angle. However, most clinicians are unfamiliar with measuring the spatial QRS-T angle, and the computerized electrocardiographic analysis tools now in use does 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 ECG and are typically reported by automated ECG devices. QRS-T angle can be easily calculated from them, and for risk prediction, it has been shown to have a strong association with the spatial QRS-T angle. Aro et al. have demonstrated a connection between a wide fQRS-T angle and both ventricular arrhythmias and abrupt cardiac mortality. An abnormal fQRS-T angle indicates the underlying myocardial ion channel disorders resulting in aberrant ventricular repolarization (Aro et al., 2012). This current study is important as it shows that fQRS-T angle is increased in patients diagnosed with MDD. Our findings support the known relationship between depression and CVD. There is only one study in the literature examining fQRS-T angle in MDD. In this very recent research (Yilmaz & Yilmaz, 2023), fQRS-T angle was found to be higher in the MDD group, similar to our study. However, when the literature is examined, it appears that cardiac abnormalities in MDD have a close relationship with inflammation (Aydin Sunbul et al., 2016). This current study is unique in that it reveals for the first time the relationship between fQRS-T angle and inflammatory markers in the drug-naive MDD group.

Stress, the most prevalent symptom of MDD, may aggravate atherosclerosis. Endothelial dysfunction and elevated platelet activation have been suggested as a possible pathophysiological mechanism between MDD and CVD. Long-term mental stress has been demonstrated to cause chronic endothelial dysfunction, which is a common occurrence in MDD patients. It has been demonstrated that endothelial dysfunction is one of the precursors of subsequent cardiovascular deterioration. Actually, a number of psychiatric disorders have been linked to oxidative stress. As previously mentioned, MDD has been linked to elevated platelet reactivity, raising the relative risk of thrombus development and blockage of an artery. One of the causal mechanisms that have been suggested to link MDD to an increased risk of CVD is inflammation, through the process of atherosclerosis. It was found that the MDD patients had higher than normal levels of inflammatory biomarkers (Dhar & Barton, 2016). Lymphocyte-related parameters have been frequently studied, especially in recent years, to indicate the possible increase in inflammation in CVDs and psychiatric disorders (Zhao et al., 2023; Su et al., 2022).

The innate immune system relies heavily on neutrophils, which are the acute phase of an inflammatory response. In contrast, lymphocytes represent the adaptive immune system and promote the induction of autoimmune inflammation, especially in the chronic inflammatory response. NLR is a biomarker of inflammation because it combines the functions of the innate and adaptive immune systems (García-Escobar et al., 2023). In a recent cohort study conducted by Zhao et al. in China, the relationship between NLR and risk of CVDs was investigated. They suggested that NLR was significantly related to the risk of total CVDs (Zhao et al., 2023). PLR and NLR are other parameters used to predict prognosis in CVDs. Tamaki et al. investigated the combined usefulness of NLR and PLR for estimating the prognosis of patients with heart failure with preserved ejection fraction admitted for acute decompensated heart failure. In that study, it is demonstrated that the combination of NLR and PLR is useful for the prediction of post discharge cardiac death in patients with acute heart failure with preserved ejection fraction (Tamaki et al., 2023). Hua et al. investigated the association between MLR with mortality and CVD mortality in United States adults. Their study demonstrated that increased baseline MLR was positively associated with a higher risk of death in United States adults. Also, it was stated that MLR was a strong independent predictor of CVD mortality in the general population (Hua et al., 2023). It has been shown in previous studies that lymphocyte-related parameters also increase in depression (Mazza et al,. 2018; Adhikari et al., 2018; Özyurt & Binici, 2018). In a meta-analysis conducted by Su et al. to investigate the relationship between depression and NLR, PLR, MLR, it was shown that patients diagnosed with depression had higher NLR levels compared to healthy controls (Su et al., 2022). In the study by Aydin-Sunbul et al., in which they compared the NLR levels of patients diagnosed with MDD and HCs, a significant positive relationship was found between the NLR level and HDRS score, and it was shown that there was a significant relationship between the CVD risk factors and NLR levels of patients diagnosed with MDD. Aydin-Sunbul et al. did not

use ECG parameters when investigating this relationship (Aydin Sunbul et al., 2016). This current study is the first to show that there is a significant positive relationship between NLR, MLR, PLR levels and depression severity and fQRS-T angle in patients diagnosed with MDD.

The cross-sectional nature of this study is the most important limitation. Investigating the effect of MDD treatment on inflammation and ECG parameters will eliminate this limitation. Since patients' blood electrolyte and thyroid hormone concentrations will change the ventricular repolarization parameters, not examining them is a limitation of this study. More extensive laboratory and detailed studies are needed for the relation between BD and frontal QRS-T angle. The inclusion of drug-naive patients diagnosed with MDD is the strongest aspect of this study.

CONCLUSION

In conclusion, this study shows that MDD has a significant relationship with increased levels of lymphocyte-related parameters such as NLR, PLR, and MLR, which are frequently investigated as novel inflammation parameters. Additionally, it has been demonstrated that cardiac parameters such as f-QRS-T angle in patients diagnosed with MDD are significantly different compared to healthy controls. It has also been suggested that there is a relationship between lymphocyte-related parameters and electrocardiographic parameters of patients diagnosed with MDD. Further studies are needed to reveal which variable affects which variable and in what direction.

Ethical Considerations: Adıyaman University Non-invasive Clinical Research Ethics Committee approved the protocol of the study. The study was conducted in accordance with good clinical practice and the declaration of Helsinki. Signed informed consent was obtained from the participants (Decision Date: 16/11/2021 and Decision Number: 2021/09-03).

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References

Adhikari, A., Dikshit, R., Karia, S., Sonavane, S., Shah, N., & De Sousa, A. (2018). Neutrophil-lymphocyte ratio and C-reactive protein level in patients with major depressive disorder before and after pharmacotherapy. *East Asian Archives of Psychiatry*, 28, 53-58.

Akdemir, A., Örsel, D. S., Dağ, İ., Türkçapar, M. H., İşcan, N., & Özbay, H. (1996). Validity-reliability and clinical use of the Hamilton depression rating scale (HDRS). *Journal of Psychiatry Psychology Psychopharmacology, 4*, 251-259.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*. American Psychiatric Publishing.

Aro, A. L., Huikuri, H. V., Tikkanen, J. T., Junttila, M. J., Rissanen, H. A., Reunanen, A., et al. (2012). QRS-T angle as a predictor of sudden cardiac death in a middle-aged general population. Europace, 14, 872-876.

Astafeva, D., Gayduk, A., Tavormina, G., Syunyakov, T., Chigareva, O., Bikbaeva, K., et al. (2023). Neuronetwork approach in the early diagnosis of depression. *Psychiatria Danubina, 35*, 77-85.

Aydin Sunbul, E., Sunbul, M., Yanartas, O., Cengiz, F., Bozbay, M., Sari, I., et al. (2016). Increased neutrophil/lymphocyte ratio in patients with depression is correlated with the severity of depression and cardiovascular risk factors. *Psychiatry Investigation, 13*, 121-126.

Dhar, A. K., & Barton, D. A. (2016). Depression and the link with cardiovascular disease. *Frontiers in Psychiatry, 7*, 33.

Dilaveris, P., Gialafos, E., Pantazis, A., Synetos, A., Triposkiadis, F., & Gialafos, J. (2001). The spatial QRS-T angle as a marker of ventricular repolarisation in hypertension. *Journal of Human Hypertension, 15*, 63-70.

García-Escobar, A., Vera-Vera, S., Tébar-Márquez, D., Rivero-Santana, B., Jurado-Román, A., Jiménez-Valero, S., et al. (2023). Neutrophil-to-lymphocyte ratio an inflammatory biomarker, and prognostic marker in heart failure, cardiovascular disease and chronic inflammatory diseases: New insights for a potential predictor of anti-cytokine therapy responsiveness. *Microvascular Research, 150*, 104598.

Gold, S. M., Köhler-Forsberg, O., Moss-Morris, R., Mehnert, A., Miranda, J. J., Bullinger, M., et al. (2020). Comorbid depression in medical diseases. *Nature Reviews Disease Primers, 6*, 69.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery & Psychiatry, 23*, 56-62.

World Health Organization. (n.d.). Depression. Retrieved from https://www.who.int/news-room/fact-sheets/detail/depression

Hua, Y., Sun, J. Y., Lou, Y. X., Sun, W., & Kong, X. Q. (2023). Monocyte-to-lymphocyte ratio predicts mortality and cardiovascular mortality in the general population. International *Journal of Cardiology, 379*, 118-126.

Katon, W. J., Lin, E. H., Russo, J., Von Korff, M., Ciechanowski, P., Simon, G., et al. (2004). Cardiac risk factors in patients with diabetes mellitus and major depression. *Journal of General Internal Medicine, 19*, 1192-1199.

Mazza, M. G., Lucchi, S., Tringali, A. G. M., Rossetti, A., Botti, E. R., & Clerici, M. (2018). Neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in mood disorders: A meta-analysis. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 84*, 229-236.

Oehler, A., Feldman, T., Henrikson, C. A., & Tereshchenko, L. G. (2014). QRS-T angle: a review. *Annals of Noninvasive Electrocardiology, 19*, 534-542.

Ozturk, B. T., Ozel, F., Yaras, T., Ekinci, B., Oktay, Y., Aysevener, E. O., et al. (2023). The relationship between cardiovascular disease risk and major depression. *Noro Psikiyatri Arsivi, 60*, 124-128.

Özyurt, G., & Binici, N. C. (2018). Increased neutrophil-lymphocyte ratios in depressive adolescents is correlated with the severity of depression. *Psychiatry Research, 268*, 426-431.

Ren, H. (2022). Effects of anxiety and depression on cardiovascular system function. *Psychiatria Danubina, 34*, 613.

Su, M., Ouyang, X., & Song, Y. (2022). Neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, and monocyte to lymphocyte ratio in depression: A meta-analysis. *Journal of Affective Disorders, 308*, 375-383.

Tamaki, S., Nagai, Y., Shutta, R., Masuda, D., Yamashita, S., Seo, M., et al. (2023). Combination of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as a novel predictor of cardiac death in patients with acute decompensated heart failure with preserved left ventricular ejection fraction: A multicenter study. *Journal of the American Heart Association, 12*, e026326.

Yilmaz, M., & Yilmaz, S. (2023). Major depressive disorder is an independent predictor of the electrocardiographic frontal QRS-T angle. *Bratislavské Lekárske Listy, 124*, 313-319.

Zhao, Y., Zhang, S., Yi, Y., Qu, T., Gao, S., Lin, Y., et al. (2023). Neutrophil-to-lymphocyte ratio as a predictor for cardiovascular diseases: a cohort study in Tianjin, China. *Journal of Human Hypertension, 37*, 576-583.

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