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Electrocardiographic Repolarization Changes in Behçet's Syndrome: A Cross-Sectional Study

ABSTRACT

Background/Aims: To evaluate electrocardiographic (ECG) markers of ventricular repolarization in Behçet's syndrome (BS) and to assess their association with clinical features, including major organ involvement and treatment characteristics.

Materials and Methods: A total of 72 patients with BS and 80 age- and sex-matched healthy controls were enrolled in this cross-sectional study, and all participants underwent a standard 12-lead ECG examination. Frontal QRS–T (fQRS–T) angle, Tp–e interval, and Tp–e/QTc ratio were measured. Clinical characteristics, including major organ involvement, disease activity, and treatment history, were recorded.

Results: Patients with BS had significantly longer Tp–e intervals ($P = .010$) and higher Tp–e/QTc ratios ($P = .014$) than controls, whereas the fQRS–T angle did not differ significantly ($P = .097$). Patients with abnormal ventricular repolarization parameters more frequently had major organ involvement and were more likely to receive immunosuppressive therapy. In multivariable analysis, vascular involvement (odds ratio (OR): 11.22, 95% CI: 2.89-44.10, $P = .001$) and ocular involvement (OR: 4.33, 95% CI: 1.27-14.72, $P = .019$) remained independently associated with abnormal ventricular repolarization parameters.

Conclusion: Patients with BS showed higher Tp–e interval and Tp–e/QTc ratio, suggesting altered ventricular repolarization, whereas fQRS–T angle was similar between groups. These alterations were more pronounced in patients with more severe disease features. Simple, noninvasive ECG markers may help identify subclinical repolarization changes and warrant further evaluation in larger, prospective studies.

Keywords: Behçet's syndrome, electrocardiography, QRS, T angle, Tp–e interval, ventricular repolarization

Introduction

Behçet's syndrome (BS) is a chronic, multisystemic inflammatory disorder characterized by recurrent oral and genital ulcers, skin lesions, ocular involvement—predominantly posterior uveitis—and neurological manifestations, reflecting its underlying vasculitic pathology that affects vessels of various sizes.[1] Although cardiac involvement is relatively uncommon, reported manifestations such as pericarditis, myocarditis, conduction disturbances, and ventricular arrhythmias are clinically significant because of their association with increased morbidity and the risk of sudden cardiac death.[2]

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Systemic inflammation has been shown to adversely affect cardiac electrophysiology, particularly by increasing heterogeneity of ventricular repolarization.[3] Proinflammatory cytokines may interfere with myocardial ion channel function, resulting in alterations of ventricular action potential duration and repolarization properties.[4]These inflammation-related electrical changes may predispose to ventricular arrhythmias, underscoring the clinical relevance of assessing ventricular repolarization in inflammatory diseases.[5]

Among electrocardiography (ECG)-derived markers, the Tp–e interval and Tp–e/QTc ratio have emerged as indices reflecting transmural dispersion of ventricular repolarization.[6] Previous studies have demonstrated prolongation of these parameters in patients with BS compared with healthy controls, suggesting the presence of subclinical, inflammation-related ventricular electrical heterogeneity even in the absence of overt cardiac involvement.[7] However, these studies primarily focused on isolated Tp–e metrics. They did not integrate markers of global electrical heterogeneity or systematically correlate ECG-derived repolarization indices with detailed disease-specific clinical phenotypes.

Another ECG-based marker, the frontal QRS–T angle (fQRS–T angle), reflects the spatial discordance between ventricular depolarization and repolarization vectors and provides an estimate of global electrical heterogeneity.[8] Widening of the fQRS–T angle has been associated with adverse cardiac outcomes in several cardiovascular conditions and has also been reported in certain chronic inflammatory diseases.[9-11]However, the extent to which the fQRS–T angle reflects inflammation-related electrical remodeling in BS remains unclear.

Despite accumulating evidence on Tp–e–based indices in BS, a comprehensive approach integrating both transmural and global markers of ventricular repolarization heterogeneity is lacking. In particular, the clinical and pathophysiological relevance of the fQRS–T angle in this context remains insufficiently explored. Addressing this gap may provide a more integrated understanding of inflammation-related electrical remodeling in BS.

MAIN POINTS

- *Patients with Behçet's syndrome (BS) exhibited higher Tp–e interval and Tp–e/QTc ratio values compared with the control group.*
- *There was no statistically significant difference in frontal QRS–T angle between patients and controls.*
- *Repolarization abnormalities were more frequent in patients with severe disease features.*
- *Electrocardiographic-derived parameters may reflect subclinical ventricular repolarization changes in BS.*

Materials and Methods

Study Design and Population

This cross-sectional observational study included 152 participants, comprising 72 patients with BS, diagnosed according to the International Study Group criteria, and 80 healthy controls, matched for age and sex. Patients were consecutively enrolled from the outpatient rheumatology clinic between September 2023 and February 2024. The control group consisted of healthy individuals with no history of systemic inflammatory or cardiovascular disease.

Individuals with a history of coronary artery disease, structural or valvular heart disease, bundle branch block, or atrial fibrillation were not included. Participants with electrolyte imbalance, diabetes mellitus, or hypertension were also excluded, as were those receiving medications known to influence cardiac conduction or repolarization, such as beta-blockers, antiarrhythmic agents, or QT-prolonging drugs. Cardiac involvement was excluded based on detailed medical history, physical examination, and available medical records. Patients with an available echocardiographic evaluation showing clinically evident structural heart disease or reduced left ventricular ejection fraction were excluded from the study.

Additionally, ECGs with inadequate technical quality—including missing or unstable T-wave axis values (e.g., flat or indeterminate T waves), poor signal quality, or artifact preventing accurate interval measurement—were excluded from the final ECG analysis.

Clinical Evaluation of Behçet's Patients

Detailed clinical assessments were performed for all patients with Behçet's. The presence or history of the following disease manifestations was recorded: oral aphthous ulcers, genital ulcers, ocular involvement, vascular involvement, and mucocutaneous findings (e.g., papulopustular or acneiform lesions, erythema nodosum). In addition, disease activity was assessed using the Behçet's Disease Current Activity Form.[12] Major organ involvement was defined as the presence of ocular, gastrointestinal (GI), vascular, or neurological involvement, consistent with established definitions in previous studies. These clinical variables were analyzed in relation to ventricular repolarization parameters to investigate potential associations between disease manifestations and cardiac electrophysiological changes.

Electrocardiographic Evaluation: Each participant underwent a standard 12-lead surface ECG (MAC 2000, GE Healthcare, Milwaukee, WI, USA) at a paper speed of 25 mm/s and an amplitude of 10 mm/mV after a 5-minute resting period in the supine position.

Tp–e Interval Measurement: The Tp–e interval was defined as the time between the peak and the end of the T wave. All measurements were performed manually across the precordial leads (V1-V6), and the median value from

these leads was used in the analysis to reduce the effect of inter-lead variability.

The end of the T wave was identified using the tangent method by determining the point at which a tangent drawn along the steepest descending portion of the terminal T wave intersected the isoelectric line.

In cases where U waves were present, the termination of the T wave was taken as the lowest point between the T and U waves to prevent overestimation. Electrocardiographic tracings with flat, notched, or poorly defined T waves that did not allow reliable measurement were excluded.

All measurements were performed independently by 2 observers (1 cardiologist and 1 internist) who were blinded to clinical data, and the average of their measurements was used for statistical analysis. Interobserver variability was evaluated using the intraclass correlation coefficient.

QTinterval and Tp–e/QTc Analysis: QTinterval and corrected QT (QTc) intervals were obtained automatically from the ECG system using a validated internal algorithm based on Bazett's formula ($QTc = QT/\sqrt{RR}$), ensuring a standardized and operator-independent evaluation.

The Tp–e/QTc ratio was then calculated by dividing the manually measured Tp–e interval by the device-derived QTc value.[13]

Frontal QRS–T Angle Measurement

Baseline parameters, including QRS axis, QRS duration, and T-wave axis, were automatically obtained from the ECG device. The fQRS–T angle represents the absolute angular difference between the QRS and T-wave axes. When this value exceeded 180°, the angle was recalculated as 360° minus the absolute difference, yielding a final value between 0° and 180°, in accordance with established methodology (Figure 1).[8] Electrocardiograms with missing or unstable T-wave axis values (e.g., flat or indeterminate T waves) were omitted from the fQRS–T analysis.

This study was approved by the Local Ethics Committee of Çukurova University (Approval No: 136/30, Date: September 01, 2023). Written informed consent was obtained from all participants before enrollment.

This study used generative AI tools (e.g., ChatGPT) for language editing and readability improvement during manuscript preparation. However, all study content was critically reviewed and revised by the authors, who take full responsibility for the final version.

Statistical Analysis

All statistical procedures were carried out using SPSS software version 23.0 (IBM SPSS Corp.; Armonk, NY, USA). The distribution of continuous variables was first examined using the Kolmogorov–Smirnov test, after which they are described either as mean ± SD or as median (interquartile range (IQR)). Categorical data are summarized as absolute counts with corresponding percentages.

Between-group comparisons were conducted using the independent samples *t*-test for normally distributed variables and the Mann–Whitney *U*-test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Correlations between the fQRS–T angle and clinical or electrocardiographic variables were evaluated using Pearson or Spearman correlation coefficients, depending on the data distribution.

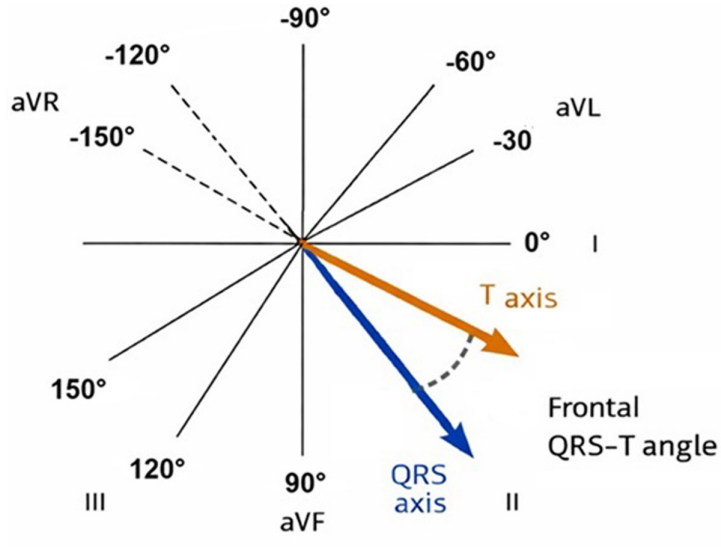

Figure 1. Measurement of the frontal QRS–T angle. Adapted from Oehler et al (2014). The schematic is consistent with the original methodology and is distributed under the terms of the Creative Commons Attribution License (CC BY).

To identify factors associated with abnormal ventricular repolarization indices, univariable logistic regression analyses were first performed. Variables with clinical relevance and/or a *P*-value < .10 in univariable analyses were considered for inclusion in the multivariable model. The clinical variables evaluated included oral aphthous ulcers, genital ulcers, cutaneous involvement, vascular involvement, ocular involvement, and disease duration. Neurological and GI involvement were excluded from the analysis due to the limited number of affected patients (fewer than 10 in each category). Given the limited number of outcome events, a forward stepwise logistic regression approach was used to identify independent predictors while minimizing the risk of model overfitting.

All analyses were conducted using 2-sided tests, and *P* values were reported to 3 decimal places; values below .05 were considered statistically significant.

Sample Size Estimation

An a priori sample size estimation was performed using G*Power software (version 3.1.9.7). To detect a between-group difference in the Tp–e interval with a 2-sided α level of 0.05 and 80% power, assuming a moderate effect size (Cohen's $d = 0.50$), a minimum of 64 participants per group was required. To account for potential exclusions related to ECG quality, a slightly larger sample was enrolled, resulting in the inclusion of 72 patients with BS and 80 control participants.

The reporting and design of this study followed the Strengthening the Reporting of Observational Studies in Epidemiology recommendations for observational studies.

Results

Patients with BS and healthy controls had similar age and sex distributions, with no statistically significant differences (Table 1). The demographic, clinical, and electrocardiographic features of the study population are summarized in Table 1. Major organ involvement was considered present in cases with vascular, ocular, GI, or neurological manifestations. Mucocutaneous involvement included oral and genital ulcers, papulopustular lesions, erythema nodosum, pathergy positivity, as well as musculoskeletal findings. The median disease duration among patients was 9.5 years (IQR, 4.25-16). All patients exhibited mucocutaneous involvement (100%). Among these manifestations, oral ulcers were the most frequent (97.2%), followed by genital ulcers (75%), papulopustular lesions (59.7%), and erythema nodosum (37.5%). Musculoskeletal involvement occurred in 54.2% of patients, and major organ involvement was identified

Table 1. Comparison of Demographic, Clinical, and Electrocardiographic Variables Between Patients with Behçet's Disease and Controls

Parameter	All Participants (n = 152)	Behçet's Syndrome (n = 72)	Healthy Controls (n = 80)	*P*
Age, years, mean ± SD	38.3 ± 10.7	40.29 ±11.7	36.5 ± 9.5	.065
Female, n (%)	80 (52.6)	37 (51.4)	43 (53.8)	.771
Comorbidities, n (%)	17 (11.2)	17 (23.6)	—	—
BMI, kg/m² mean ± SD	23.6 ± 3.6	24.1 ± 4.1	23.5 ± 2.2	.301
Current smoker, n (%)	51 (33.6)	30 (41.7)	21 (26.3)	.044
Smoking duration, years, mean ± SD	11.4 ± 6.1	11.9 ± 6.5	10.6 ± 5.3	.446
Heart rate, bpm, mean ± SD	76.6 ± 11	76.2± 12.4	76.9 ± 9.6	.580
Tp–e interval, ms, mean ± SD	76.63 ± 17.17	80.46 ± 20.09	73.19 ± 13.25	.010
Frontal QRS–T angle, degrees, median (IQR)	19 (0-129)	23 (0-129)	18.5 (0-70)	.097
QT interval, ms, mean ± SD	366.85 ± 27.42	367.29 ± 29.95	366.45 ± 25.12	.851
QTc interval, ms, mean ± SD	409.81 ± 40.34	413.54 ± 29.30	406.45 ± 48.11	.281
Tp–e/QTc ratio	0.19 ± 0.04	0.20 ± 0.05	0.18 ± 0.03	.014
Abnormal ventricular repolarization parameters, n (%)				
Tp–e > 100 ms	20 (13.2)	17 (23.6)	3 (3.8)	.000
Tp–e/QTc > 0.25	17 (11.2)	14 (19.5)	3 (3.8)	.002
Frontal QRS–T > 45°	19 (12.5)	12 (16.7)	7 (8.8)	.141
Disease activity, n (%)	—		—	—
Inactive	—	40 (55.6)	—	—
Low–moderate	—	24 (33.3)	—	—
High	—	8 (11.1)	—	—

Comorbidities included hypothyroidism, asthma, migraine, and other chronic medical conditions not meeting study exclusion criteria.
BMI, body mass index; bpm, beats per minute; IQR, interquartile range; ms, milliseconds; n, number; QTc, corrected QT interval; Tp–e, T peak to T end interval.

in 70.8%, including vascular (26.4%), ocular (54.2%), GI (4.2%), and neurological involvement (4.2%). The majority of patients were receiving colchicine therapy (86.1%), and nearly half were on immunosuppressive therapy (47.2%; azathioprine, 44.4%; methotrexate, 5.6%). Additionally, 25% of patients were receiving biologic agents (adalimumab, 12.5%; infliximab, 12.5%).

Patients with BS demonstrated a significantly prolonged Tp-e interval compared to healthy controls (80.46 ± 20.09 ms vs. 73.19 ± 13.25 ms, *P* = .010). Although the frontal QRS–T angle appeared higher in patients with BS (23 (0-129)°) than in controls (18.5 (0-70)°), this difference was not statistically significant (*P* = .097) (Figure 2). QT and QTc intervals were comparable across groups. However, the Tp–e/QTc ratio was significantly elevated in the patient group (0.20 ± 0.05 vs. 0.18 ± 0.03, *P* = .014) (Table 1).

For comparative analysis, patients with BS were categorized into 2 subgroups: those with at least 1 abnormal ventricular repolarization parameter (Tp–e > 100 ms, Tp–e/QTc > 0.25, or frontal QRS–T angle > 45°; n = 29) and those with all 3 parameters within the normal range (n = 43). These thresholds were chosen because each parameter, when exceeding the stated cut-off, has been reported to be independently associated with a higher risk of ventricular arrhythmias and sudden cardiac death in prior investigations.[14-16] The group with abnormal ventricular repolarization was characterized by a significantly greater prevalence of major organ involvement (*P* = .040), notably vascular involvement (*P* = .018), and more frequent use of immunosuppressive therapy (*P* = .020) (Table 2). Table 2 presents the demographic, clinical, and laboratory features of these subgroups.

In univariable logistic regression analysis, male sex, vascular involvement, ocular involvement, and immunosuppressive therapy were associated with abnormal ventricular repolarization parameters. In contrast, no significant relationship was observed for C-reactive protein levels, smoking status, or overall disease activity (Table 3).

A forward stepwise logistic regression approach was used to identify variables independently associated with abnormal ventricular repolarization parameters. In the multivariable model, vascular involvement (odds ratio (OR): 11.22, 95% CI: 2.89-44.10, *P* = .001) and ocular involvement (OR: 4.33, 95% CI: 1.27-14.72, *P* = .019) remained independently associated with repolarization abnormalities.

Discussion

In this study, patients with BS had a higher Tp–e interval and a higher Tp–e/QTc ratio than healthy controls. In contrast, the fQRS–T angle did not differ significantly between the groups. Abnormal repolarization parameters were more common among patients with vascular and ocular involvement and among those receiving immunosuppressive therapy.

The findings are broadly consistent with previous studies showing increased Tp–e-derived indices in BS and other systemic inflammatory diseases.[17,18] Most previous studies, however, focused on isolated ECG parameters. By simultaneously evaluating Tp–e-derived indices and the fQRS–T angle in the same cohort, the study offers a more integrated perspective on ventricular repolarization abnormalities in BS. To the best of current knowledge, this is among the first studies to evaluate the fQRS–T angle in BS.

One notable finding of this study was the absence of a significant difference in the fQRS–T angle. The frontal

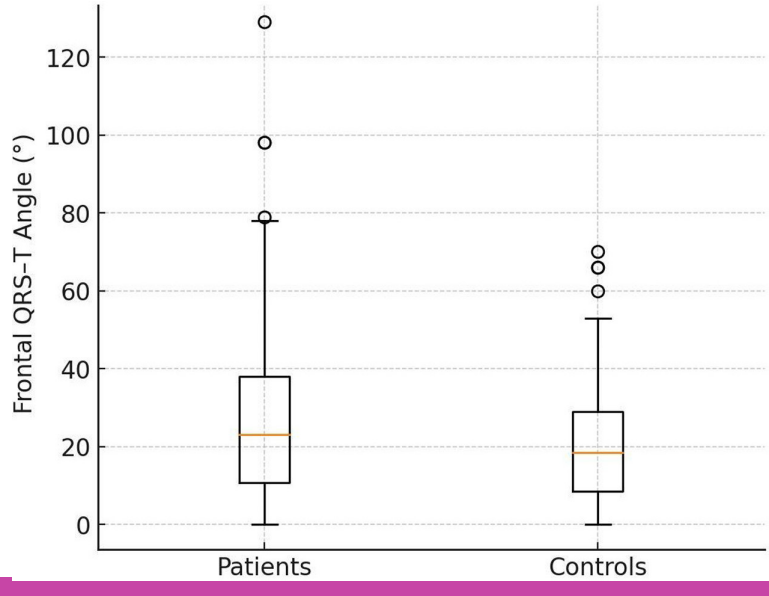

Figure 2. Comparison of frontal QRS–T angle between patient and control groups

Table 2. Comparison of Behçet's Syndrome Patients with and Without Elevated Ventricular Repolarization Parameters

Parameter	Abnormal Parameter(s) Present (n = 29)	All Parameters Normal (n = 43)	*P*
Age, years, mean ± SD	39.3 ± 11.2	40.9 ± 12.1	.575
Male sex, n (%)	19 (65.5)	16 (37.2)	.018
Body mass index, kg/m^2, ± SD)	24.3 ± 6.5	24.8 ± 3.4	.673
Comorbidities, n (%)	7 (24.1)	10 (23.3)	.932
Disease duration, years, median (min-max)	11 (1-49)	9 (1-26)	.679
ESR, mm/h, median (min-max)	11 (2-36)	8 (2-39)	.554
CRP, mg/L, median (min-max)	3.6 (1-20)	3 (0.6-21.6)	.717
Current smoker, n (%)	16 (55.2)	15 (34.9)	.209
Smoking duration, years, mean ± SD	10.06 ± 7	13.13 ± 6.25	.169
Mucocutaneous involvement, n (%)	29 (100)	43 (100)	—
Oral ulcer, n (%)	28 (96.6)	42 (97.7)	.776
Genital ulcer, n (%)	24 (82.8)	30 (69.8)	.212
Papulopustular lesions, n (%)	21 (72.4)	22 (51.2)	.071
Erythema nodosum, n (%)	11 (37.9)	16 (37.2)	.951
Pathergy positivity, n (%)	15 (51.7)	18 (41.9)	.410
Musculoskeletal involvement, n (%)	16 (55.2)	23 (53.5)	.888
Major organ involvement, n (%)	26 (89.7)	25 (58.1)	.040
Vascular involvement, n (%)	12 (41.4)	7 (16.3)	.018
Ocular involvement, n (%)	19 (65.5)	20 (46.5)	.112
Gastrointestinal involvement, n (%)	2 (6.9)	1 (2.3)	.561
Neurological involvement, n (%)	1 (3.5)	2 (4.7)	1.000
Colchicine use, n (%)	23 (79.3)	39 (90.7)	.171
Immunosuppressive therapy, n (%)	20 (69.0)	14 (32.6)	.020
Biologic therapy, n (%)	8 (27.6)	10 (23.3)	.677
Active disease, n (%)	15 (51.7)	17 (39.5)	.103

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; n, number.

QRS–T angle reflects the spatial relationship between ventricular depolarization and repolarization and is considered a marker of global electrical heterogeneity. Increased values have been associated with myocardial remodeling, fibrosis, ventricular arrhythmias, and adverse cardiovascular outcomes in various cardiac disorders.[16,19,20] In contrast, Tp–e-derived indices are thought to reflect transmural repolarization abnormalities more directly.[21] This suggests that BS mainly involves selective repolarization abnormalities, not broad disruptions in global ventricular electrical organization. The lack of change in frontal QRS–T angle refines the understanding of the syndrome's electrophysiological profile and may indicate that Tp–e-based parameters are more sensitive for detecting early or subclinical ventricular electrical involvement.

This interpretation is also compatible with the known cardiovascular pathology of BS. Although cardiac involvement in BS may range from pericarditis and myocarditis to intracardiac thrombosis and endomyocardial fibrosis, subclinical myocardial involvement may be more closely associated with chronic inflammation, endothelial dysfunction, and microvascular abnormalities than with extensive structural remodeling.[22] Such changes may be sufficient to influence Tp–e-derived parameters without necessarily producing a measurable change in the fQRS–T angle. In this respect, the negative fQRS–T finding does not weaken the study; rather, it helps define the pattern of ECG abnormalities observed in this cohort.

The association between abnormal repolarization parameters and vascular involvement is clinically relevant. Vascular disease in BS usually reflects a more severe inflammatory phenotype. It is plausible that this systemic vascular-inflammatory burden is also accompanied by subtle changes in myocardial electrical activity. A similar interpretation may apply to ocular involvement. Ocular manifestations, including posterior uveitis and retinal vasculitis, constitute a major form of organ involvement in BS and are typically associated with greater disease severity.[23,24] Although the present study cannot establish a mechanistic link, the higher frequency of repolarization abnormalities in these patients may indicate that ECG changes are more evident in those with more severe systemic disease. This interpretation is supported by the findings of Varkal et al, who demonstrated an association between vascular involvement and diastolic dysfunction in patients with BS. Although different markers of subclinical cardiac involvement were evaluated, both studies identified vascular disease as a feature associated with cardiac abnormalities.[25]

The association with immunosuppressive therapy should also be interpreted carefully. In routine practice, immunosuppressive agents are more often used in patients with major organ involvement or more severe disease, especially vascular disease.[26]Therefore, the observed association is likely to reflect disease severity and confounding by indication rather than a direct treatment-related effect on ventricular repolarization. This interpretation is supported by previous studies showing that cardiovascular involvement in BS is more common among

Table 3. Factors Associated with Ventricular Repolarization Parameters in Behçet's Syndrome: Univariate and Multivariate Analyses

Variable	Univariate OR (95% CI)	Univariate *P*	Multivariate OR (95% CI)	Multivariate *P*
Age, years	0.99 (0.95-1.03)	.570	—	—
BMI, kg/m^2	0.929 (0.820-1.052)	.247	—	—
Male sex	3.023 (1.153-7.924)	.024	—	—
CRP	1.015 (0.900-1.145)	.806	—	—
Smoking	0.935 (0.828-1.056)	.193	—	—
Vascular involvement	7.093 (2.173-23.157)	.001	11.22 (2.90-44.10)	.001
Ocular involvement	2.400 (0.906-6.356)	.078	4.33 (1.28-14.72)	.019
Immunosuppressive therapy	4.603 (1.672-12.676)	.003	—	—
Disease activity	2.33 (0.87-6.21)	.092	—	—

Multivariable analysis was performed using a forward stepwise logistic regression approach. Dashes indicate variables not retained in the final forward stepwise multivariable model.
BMI, body mass index; CRP, C-reactive protein; OR, odds ratio.

patients with severe systemic disease manifestations and that immunosuppressive therapy constitutes a cornerstone of treatment for cardiovascular involvement.[27,28] Furthermore, some studies have reported an inverse association between azathioprine use and markers of subclinical atherosclerosis in BS, suggesting that immunosuppressive therapy itself is unlikely to be the primary driver of adverse cardiovascular changes.[29]Accordingly, immunosuppressive treatment in the cohort may be better viewed as a marker of severe disease rather than an independent explanation for the observed ECG abnormalities.[24,30]

Similarly, the association with male sex is in keeping with the recognized tendency toward a more severe phenotype and more frequent vascular or cardiovascular involvement among men with BS.[25,31] This observation supports the idea that repolarization abnormalities may cluster in more clinically severe subgroups rather than being uniformly distributed across the disease spectrum.

The findings are consistent with a growing body of evidence indicating that cardiovascular involvement in BS may extend beyond overt clinical manifestations. Previous studies have demonstrated subclinical cardiac dysfunction by tissue Doppler echocardiography, as well as increased carotid intima-media thickness, impaired flow-mediated dilation, and endothelial alterations in patients without clinically apparent cardiovascular disease.[32-35] Together, these observations support the concept that clinically silent cardiovascular involvement may represent an underrecognized component of BS and may be detectable using different complementary modalities.

From a clinical perspective, the Tp–e interval and the Tp–e/QTc ratio are simple, widely available ECG parameters. The findings suggest that these markers may capture subclinical repolarization changes in selected patients with BS, particularly those with severe disease features. In this context, ECG-derived repolarization abnormalities may serve as a practical marker prompting referral for further cardiologic assessment, including echocardiographic evaluation when clinically indicated. However, given the cross-sectional design and the absence of data on arrhythmic outcomes, these findings should be interpreted as supportive rather than definitive.

Strengths and Limitations

A strength of this study is the combined evaluation of fQRS–T angle, Tp–e interval, and Tp–e/QTc ratio in a clinically characterized Behçet cohort. This allowed them to compare markers that may reflect different aspects of ventricular electrical heterogeneity and to relate them to disease phenotype.

Certain limitations should be noted. First, the cross-sectional, single-center design limits causal inference and may reduce the generalizability of the findings. Second, the relatively modest sample size may have limited the statistical power to detect weaker associations. Third, detailed cardiac imaging findings were not incorporated into the present analysis; therefore, the structural correlates of the observed ECG changes could not be assessed. Future studies integrating electrocardiographic parameters with echocardiographic findings and advanced cardiac imaging modalities, such as cardiac magnetic resonance imaging, may provide a more comprehensive evaluation of subclinical cardiac involvement in BS. Finally, no longitudinal follow-up or arrhythmic outcome data were available. Therefore, the clinical and prognostic significance of the observed ventricular repolarization abnormalities remains uncertain, and future prospective studies are needed to determine whether these ECG findings are associated with subsequent arrhythmic events.

Conclusion

In conclusion, patients with BS demonstrated increased Tp–e interval and Tp–e/QTc ratio, whereas the frontal QRS–T angle remained similar to controls. These findings suggest altered ventricular repolarization, predominantly transmurally. Repolarization abnormalities were more frequently observed in patients with more severe disease features.

Tpe-derived parameters may provide simple and non-invasive markers of subclinical electrical changes in BS. These findings should be interpreted with caution, particularly given the study's cross-sectional design. Further prospective studies are needed to clarify their clinical significance.

Data Availability Statement: *The data that support the findings of this study are available on request from the corresponding author.*

Artificial Intelligence Usage Statement: *During the preparation of this manuscript, ChatGPT (OpenAI, GPT-4) was used for language editing and improvement of readability. All content was critically reviewed and verified by the authors, who take full responsibility for the final version of the manuscript.*

Ethics Committee Approval: *Ethical committee approval was received from the Ethics Committee of Çukurova University Faculty of Medicine (Approval No.: 136/30; Date: September 1, 2023).*

Informed Consent: *Written informed consent was obtained from the participants who agreed to take part in the study.*

Peer-review: *Externally peer-reviewed.*

Author Contributions: *Concept – Z.T., R.E.A., İ.T.; Design – K.A, İ.T.; Supervision – K.A., İ.T.; Resources – R.E.A., İ.T.; Materials – Z.T.; Data Collection and/or Processing – Z.T., R.E.A.; Analysis and/or Interpretation – K.A.; Literature Search – Z.T., G.V., R.E.A.; Writing Manuscript – Z.T., İ.T.; Critical Review – Z.T., K.A., G.V., R.E.A., İ.T.*

Declaration of Interests: *The authors have no conflicts of interest to declare.*

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