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Original Article

MEDITERRANEAN DIET ADHERENCE AND CHRONOTROPIC RESPONSE IN PATIENTS UNDERGOING EXERCISE TESTING

SEDA ELÇİM YILDIRIM[1], TARIK YILDIRIM[1]

[1] Balıkesir University, Faculty of Medicine, Department of Cardiology, Balıkesir, Türkiye

ABSTRACT

Introduction: Adherence to the Mediterranean diet has been associated with favorable cardiovascular and metabolic outcomes. However, its relationship with chronotropic response during exercise testing remains insufficiently explored. This study aimed to evaluate the association between Mediterranean Diet Adherence Score (MEDAS) and exercise test parameters, particularly chronotropic response, in patients undergoing exercise testing.

Methods: This single-center, prospective observational study included patients referred for exercise testing in a cardiology outpatient clinic. Adherence to the Mediterranean diet was assessed using the MEDAS questionnaire. Exercise test parameters, including exercise duration, peak heart rate, heart rate reserve, chronotropic index, and double product, were recorded using the standard Bruce protocol. Laboratory parameters were obtained from fasting blood samples. Patients were categorized into low and high MEDAS groups based on the median score. Multivariable linear regression analysis was performed to identify determinants of chronotropic index.

Results: A total of 312 patients were included. Patients with higher MEDAS scores demonstrated higher chronotropic index and heart rate reserve values compared with those with lower adherence. Fasting glucose, triglyceride levels, and triglyceride–glucose index tended to be lower in the high MEDAS group. MEDAS score showed a weak but significant negative correlation with body mass index. In multivariable analysis, beta-blocker and calcium channel blocker use were the strongest determinants of chronotropic index, while MEDAS score was not independently associated after adjustment.

Conclusion: Higher adherence to the Mediterranean diet is associated with favorable trends in chronotropic response and cardiometabolic parameters in patients undergoing exercise testing. MEDAS may serve as a practical complementary tool for lifestyle-based cardiovascular risk assessment.

Keywords: Mediterranean diet; MEDAS; Chronotropic index; Exercise testing; Cardiovascular risk

INTRODUCTION

The Mediterranean diet (MD) is one of the most extensively studied dietary patterns for the prevention of cardiovascular diseases, largely due to its antiinflammatory and antioxidant properties (1,2). Adherence to the Mediterranean diet, commonly assessed using the Mediterranean Diet Adherence Score (MEDAS), has been reported to exert favorable effects on high density lipoprotein cholesterol levels, waist circumference, uric acid and glycemic parameters (3,4). Large scale epidemiological and clinical studies conducted in recent years have demonstrated that high adherence to the Mediterranean diet is associated with a reduced prevalence of obesity, dyslipidemia, insulin resistance and metabolic syndrome (5,6).

Current literature emphasizes that the benefits of the Mediterranean diet extend beyond traditional cardiometabolic risk factors and include associations with low grade chronic inflammation and autonomic nervous system dysfunction. Studies using nuclear magnetic resonance spectroscopy have shown that higher MEDAS scores are associated with less atherogenic lipoprotein subfractions and improved insulin sensitivity. Moreover, adherence to the Mediterranean diet has been suggested to reduce metabolic and vascular burden in chronic inflammatory conditions (7–9).

Nevertheless, the relationship between Mediterranean diet adherence and exercise capacity, chronotropic response, and laboratory parameters in outpatient individuals undergoing exercise testing has been investigated in only a limited number of studies (10–12). Therefore, the present study aimed to evaluate the association between MEDAS score and exercise test parameters as well as laboratory findings in patients undergoing exercise testing.

METHODS

This single center, prospective observational study included patients who underwent exercise testing for clinical indications in the cardiology outpatient clinic. Patients with acute coronary syndrome, advanced valvular heart disease, significant arrhythmias or contraindications to exercise testing were excluded. Height and weight measurements were obtained and body mass index (BMI) was calculated.

All patients underwent exercise testing using the standard Bruce protocol. Exercise duration, peak heart rate, heart rate reserve, chronotropic index and double product were recorded. Biochemical and lipid parameters were measured from fasting

Corresponding Author: Seda Elçim Yıldırım. Department of Cardiology Faculty of Medicine, Balıkesir University Balıkesir, Türkiye
E-mail: sedaelcimdurusoy@gmail.com
ORCID: 0000-0001-5175-0491

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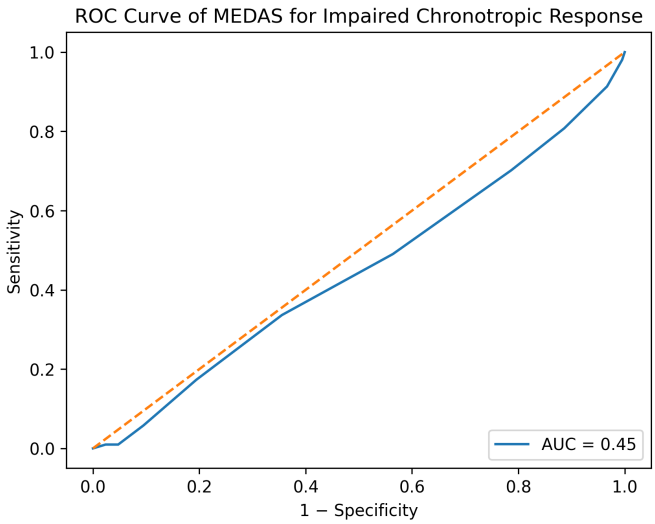
Figure 1. Receiver Operating Characteristic (ROC) Curve of MEDAS for Impaired Chronotropic Response



The ROC curve illustrates the ability of the Mediterranean Diet Adherence Score (MEDAS) to predict impaired chronotropic response during exercise testing. Sensitivity is plotted against 1 − specificity. The area under the curve (AUC) indicates no clinically meaningful discriminative ability of MEDAS as a standalone parameter.

blood samples. Adherence to the Mediterranean diet was assessed using the MEDAS questionnaire.

Definition of impaired chronotropic response: For the ROC analysis, impaired chronotropic response (chronotropic incompetence) was defined a priori as a chronotropic index <0.80 in participants not receiving beta-blocker therapy and <0.62 in those receiving beta-blockers, consistent with accepted criteria. This dichotomous definition was used to construct the ROC curve. Medication exposure was recorded at the class level (beta-blocker use: yes/no; calcium channel blocker use: yes/no). Data on specific subclasses (e.g., cardioselective vs nonselective beta-blockers; dihydropyridine vs nondihydropyridine calcium channel blockers) were not consistently available; therefore, analyses by medication subtype were not performed. The study protocol was reviewed and approved by the Balıkesir University Non-Interventional Research Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study.

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation, whereas non-normally distributed variables are expressed as median (interquartile range). Group comparisons were performed using the independent samples t-test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. The association between MEDAS score and BMI was evaluated using Pearson correlation analysis. A p value < 0.05 was considered statistically significant. MEDAS was analyzed both categorically and continuously. Categorization by the median (≤6 vs >6) was used to facilitate clinically interpretable group comparisons, whereas modeling MEDAS as a continuous variable in regression analyses preserved information and reduced the loss of statistical power associated with dichotomization.

Table 1. Demographic and Clinical Characteristics of the Study Population

Variable	Low MEDAS (≤6)	High MEDAS (>6)	p value
Age (years)	52.20 ± 11.55	53.37 ± 11.81	0.40
Body mass index (kg/m²)	28.35 ± 3.85	27.62 ± 4.94	0.15
Sex (Male/Female), n (%)	78/42 (%65/%35)	74/48 (%61/%39)	0.48
Hypertension, n (%)	64 (%53)	58 (%48)	0.42
Diabetes mellitus, n (%)	38 (%32)	34 (%28)	0.51
Coronary artery disease, n (%)	29 (%24)	26 (%22)	0.67
Hyperlipidemia, n (%)	71 (%59)	69 (%57)	0.78

RESULTS

The median MEDAS score of the study population was calculated as 6. Accordingly, patients were classified into a low adherence group (MEDAS ≤6) and a high adherence group (MEDAS >6). There were no statistically significant differences between the two groups in terms of age, sex distribution or body mass index (Table 1).

When clinical comorbidities were evaluated, no significant differences were observed between the low and high MEDAS groups with respect to the prevalence of hypertension, diabetes mellitus, coronary artery disease or hyperlipidemia. These findings indicate that the cardiovascular risk profiles of the groups were comparable (Table 1).

Regarding exercise test parameters, the high MEDAS group exhibited higher chronotropic index and heart rate reserve values compared with the low MEDAS group. Exercise duration and peak heart rate were similar between groups (Table 2).

Table 2. Exercise Test Parameters According to MEDAS Groups

Parameter	Low MEDAS (≤6)	High MEDAS (>6)	p value
Exercise duration (min)	5.91 ± 1.92	5.67 ± 1.97	0.42
Peak heart rate (beats/min)	148.24 ± 14.68	145.54 ± 14.45	0.31
Heart rate reserve	42.98 ± 15.43	43.79 ± 14.14	0.68
Chronotropic index	0.66 ± 0.31	0.69 ± 0.20	0.21

In the evaluation of laboratory parameters, fasting glucose levels, triglyceride concentrations and triglyceride–glucose index values were lower in the high MEDAS group. High density lipoprotein cholesterol levels tended to be higher in the high MEDAS group. However, none of these differences reached statistical significance (Table 3).

Correlation analysis revealed a weak but statistically significant negative association between MEDAS score and BMI ($r = -0.11$; $p = 0.045$).

The ability of the MEDAS score to predict an impaired exercise response was evaluated using receiver operating characteristic (ROC) analysis. The area under the ROC curve (AUC) was

Table 3. Laboratory Parameters According to MEDAS Groups

Parameter	Low MEDAS (≤6)	High MEDAS (>6)	p value
Glucose (mg/dL)	109.26 ± 29.72	103.56 ± 21.43	0.077
Triglycerides (mg/dL)	156.53 ± 91.02	142.22 ± 77.31	0.16
HDL cholesterol (mg/dL)	53.69 ± 14.23	55.16 ± 12.80	0.36
Triglyceride–glucose index (TyG)	8.81 ± 0.59	8.90 ± 0.61	0.21
Creatinine (mg/dL)	0.89 ± 0.18	0.87 ± 0.16	0.34

calculated as 0.51, indicating no clinically meaningful discriminative ability of MEDAS when used alone (Figure 1).

Multivariable linear regression analysis was performed to determine the determinants of heart rate response. After adjusting for medication use and clinical variables, medication use—particularly heart rate–modifying agents—showed the largest effect estimates in the multivariable model, although statistical significance was not reached (Table 4). Beta-blocker use was associated with a lower chronotropic index, whereas calcium channel blocker use showed a similar but weaker direction of effect. When MEDAS score was included in the model as a continuous variable, it did not show an independent association with chronotropic index after adjustment for age, sex, BMI and medication use. Likewise, ACE inhibitor/ARB and statin use were not significantly associated with chronotropic index. The overall explanatory power of the model was moderate, suggesting that a substantial proportion of the variability in chronotropic response was driven by pharmacological factors. These findings underscore the importance of considering heart rate modifying medications when interpreting chronotropic response during exercise testing.

Table 4. Multivariable Linear Regression Analysis of Chronotropic Index

Variable	B (beta)	SE	95% CI	p value
MEDAS (continuous)	0.002	0.008	-0.014 – 0.017	0.816
Age	-0.001	0.001	-0.004 – 0.001	0.341
Sex (Male)	0.028	0.032	-0.035 – 0.091	0.387
BMI (kg/m²)	-0.000	0.004	-0.008 – 0.007	0.918
Beta-blocker	-0.025	0.041	-0.105 – 0.055	0.545
Calcium channel blocker	0.047	0.062	-0.075 – 0.169	0.448
ACE-I / ARB	-0.055	0.034	-0.122 – 0.011	0.101
Statin	0.060	0.039	-0.016 – 0.137	0.123

Model fit: $R^2 = 0.022$, N = 312

DISCUSSION

The principal findings of the present study indicate that individuals with higher MEDAS scores tend to exhibit more favorable cardiometabolic and functional profiles. These observations may be explained by the regulatory effects of the Mediterranean diet on inflammation and autonomic nervous system function.

The Mediterranean diet, characterized by high consumption of olive oil, vegetables, fruits, fish and nuts, is rich in polyphenols and omega-3 fatty acids. These components contribute to the suppression of inflammatory markers such as C-reactive protein, interleukin-6, and tumor necrosis factor-alpha. Recent studies have demonstrated that higher MEDAS scores are associated with lower uric acid levels, smaller waist circumference, and higher HDL cholesterol concentrations (2–4). Through the attenuation of inflammation, these effects may lead to improved endothelial function and enhanced exercise tolerance.

In parallel, the role of autonomic nervous system balance in exercise response has gained increasing attention. Parameters such as chronotropic index and heart rate reserve reflect sympathovagal balance. Previous studies have reported that high adherence to the Mediterranean diet is associated with increased parasympathetic activity and reduced sympathetic tone (10,11). The more favorable chronotropic response observed in the high MEDAS group in our study is consistent with this proposed mechanism.

The limited discriminative ability of MEDAS observed in ROC analysis suggests that this score may be more appropriately used as a complementary parameter rather than a standalone diagnostic tool. Given that MEDAS is a lifestyle adherence score rather than a diagnostic biomarker, the ROC analysis should be interpreted as exploratory. The low AUC indicates that MEDAS alone cannot be used to identify impaired chronotropic response at the individual patient level; instead, MEDAS may be more relevant as a complementary measure reflecting broader cardiometabolic and autonomic profiles. Nevertheless, considering the long term cardiovascular benefits mediated through inflammation and autonomic function, MEDAS may still serve as a valuable guide in clinical practice (14).

In this study, adherence to the Mediterranean diet was associated with favorable trends in cardiometabolic and functional parameters among outpatient individuals undergoing exercise testing. The absence of a significant difference in BMI between MEDAS groups suggests that the beneficial effects of the Mediterranean diet cannot be attributed solely to weight loss.

Chronotropic index and heart rate reserve, which are assessed during exercise testing, are important indicators of autonomic nervous system function (12,15). The more favorable values observed in the high MEDAS group support the hypothesis that the Mediterranean diet may positively influence autonomic balance and cardiovascular adaptation.

The favorable trends observed in metabolic parameters are consistent with the well established benefits of the Mediterranean diet on insulin resistance, lipid metabolism, and inflammation. Collectively, these findings support the notion that MEDAS may reflect not only dietary habits but also functional cardiovascular status in clinical practice (7–9). This study has several limitations, including its single-center design and the potential influence of unmeasured lifestyle factors, which should be considered when interpreting the results. Although the study was conducted prospectively, its observational nature precludes causal inference and the findings should be interpreted as associations.

CONCLUSION

Adherence to the Mediterranean diet tends to be associated with a more favorable cardiometabolic and functional profile in outpatient individuals undergoing exercise testing, independent of body weight. The MEDAS score may be considered a simple and practical complementary tool for lifestyle based cardiovascular risk assessment in routine clinical practice.

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Ethics Committee Approval: The study protocol was reviewed and approved by the Balıkesir University Non-Interventional Research Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants prior to inclusion in the study.

Authorship Contributions: Concept – SEY ; Design – SEY; Supervision – SEY ; Resource – SEY; Materials – SEY; Data collection &/or processing – TY; Analysis &/or interpretation – TY; Literature search – SEY; Writing – TY; Critical review – TY.

Conflict of Interest: The authors declare that there is no conflict of interest related to this study.

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