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Original article

Physical exercise may improve problem-solving skills and emotional intelligence in patients with relapsing-remitting multiple sclerosis: A cross-sectional study

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ABSTRACT

Background: Multiple sclerosis is a disease that can reduce the quality of life with a physical disability, neuropsychiatric disorders, and cognitive dysfunctions. Therefore, multiple sclerosis treatment should include treatments for cognitive and neuropsychiatric disorders and pharmacological treatments. This study aimed to examine the effects of exercise on neuropsychiatric disorders, problem-solving skills, and emotional intelligence in multiple sclerosis patients.
Methods: Thirty-six female relapsing-remitting multiple sclerosis patients aged between 18 and 45 years, with an Expanded Disability Status Scale between 1 and 3, who were diagnosed with definitive multiple sclerosis according to the revised McDonald criteria were included in the study. Participants completed outcome measures before and after the 12-week exercise program. Demographic/clinical information of the participants was obtained at baseline, neurological examinations were performed, and graded exercise testing on a bicycle ergometer was performed to determine aerobic capacity. Short Form-12 Version 2, Hospital Anxiety and Depression Scale, Modified Fatigue Impact Scale, Problem-Solving Inventory, Emotional Intelligence Scale were evaluated before and after the exercise program of the participants.
Results: While a significant increase was observed in the HRpeak values of the participants after the exercise ($p < 0.05$), the $VO2_{max}$ values also showed a highly significant difference compared to the pre-treatment values. ($p < 0.01$). While a significant difference was detected in the mental subparameter of Short Form-12 ($p < 0.05$), a high level of significant difference was found in the physical subparameter ($p < 0.01$). While no significant difference was observed in the Hospital Anxiety and Depression Scale anxiety subparameter ($p > 0.05$), a significant difference was found in the depression subparameter ($p < 0.01$). There was a significant difference in Modified Fatigue Impact Scale physical and cognitive subparameters compared to pre-treatment ($p < 0.01$). A significant difference was observed in the Emotional Intelligence Scale total score after the treatment ($p < 0.01$).
Conclusions: The results of our study showed that exercise in relapsing-remitting multiple sclerosis patients provided significant improvements in emotional intelligence, improved neuropsychiatric parameters, and increased problem-solving skills. In addition, to the best of our knowledge, this study is the first study in the literature to investigate the effect of physical activity exercises on problem-solving skills in multiple sclerosis patients.

Abbreviations: MS, multiple sclerosis; MRI, magnetic resonance imaging; EI, emotional intelligence; RRMS, relapsing-remitting multiple sclerosis; EDSS, expanded disability status scale; PAR-Q, physical activity readiness questionnaire; HRR, heart rate reserve; HRpeak, maximum heart rate; VO2peak, peak oxygen consumption; SF-12v2, short form-12 version 2; HAD, hospital anxiety and depression scale; MFIS, modified fatigue impact scale; PSI, problem-solving inventory; EIS, emotional intelligence scale; VO_{2max}, maximum aerobic capacity.

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1. Introduction

In multiple sclerosis (MS), there are white matter pathology, cortical atrophy, cortical lesions, and microstructural abnormalities in gray matter that affect structural and functional connectivity. Most lesions in the brain are asymptomatic on routine physical examination, but these lesions can cause marked cognitive, emotional, and behavioral changes in patients (Di Filippo et al., 2018). An anatomical study using diffusion imaging and resting-state functional magnetic resonance imaging (MRI) demonstrated that disconnection in the default mode and attentional networks disrupts the compensatory mechanisms necessary for the brain to overcome widespread structural damage in the early period, and this provides an adequate explanation for the cognitive dysfunction that can be seen even in the early stages of the disease (Louapre et al., 2014). From the early stages of the disease, fluctuations are observed in executive functions such as continuity of attention, working memory, conceptual-abstract reasoning, information processing speed, planning, language, and visuospatial perception (Wojcik et al., 2019). These fluctuations can negatively affect daily living activities and the ability to cope with daily life problems (Artemiadis et al., 2020).

In addition to cognitive impairment, Emotional Quotient and Intelligence Quotient impairment can also be seen in MS patients (Bobholz and Rao, 2003; Ghajarzadeh et al., 2014). Emotional intelligence (EI) is a skill that facilitates the individual's harmony and peace with him/-herself, other people, the environment, the achievement of life goals, and coping with difficulties (Palmer et al., 2002). The MS disease process and the emotional response to this process affect the individual's performance in all aspects. Also, negative emotions can lead to not achieving the desired compatibility, increased stress, and impairment in the regulation of the immune system (Basińska et al., 2013), which may worsen the disease's clinical course. The cognitive-neuropsychological state, which is not considered like other neurological deficits in MS patients, has an important place in improving the quality of life. Studies suggest that MS patients have a significantly lower ability to cope with stress (Ožura et al., 2013).

In recent years, non-drug approaches have been the subject of numerous studies due to the lack of definitive pharmacological treatment for cognitive impairment, which is common in MS patients, or the side effects of the agents used in the studies (He et al., 2013; Das Nair et al., 2012; Rosti-Otajärvi et al., 2014). Although the positive effects of physical activity on cognitive functions have been shown, the mechanism of action is not fully known. Among the possible mechanisms of action, facilitation in synaptogenesis, reduction in cardiovascular risk factors, increased cerebral blood flow, increased neurotrophin levels, improved vascularization, reduction in systemic inflammation, and decreased defective protein accumulation have been suggested (Radak et al., 2010; Intlekofer et al. 2013; Chodzko-Zajko et al., 2009; Grodstein et al., 2007). Neurotrophins such as brain-derived neurotrophic factors or neuronal growth factors are associated with increased neuroplasticity and neurovascularization in many brain areas (Vaynman et al., 2005). A meta-analysis on the effect of exercise on cognitive performance in MS patients reported not enough clinical studies to conclude in this area (Motl and Gosney, 2008).

Since the most common problem in MS cases is neuropsychiatric problems, there is little information about EI and problem-solving skills in MS cases. In addition, we did not find any research in the literature examining the effect of exercise on emotional intelligence (EI) and problem-solving skills in individuals with MS. This study examines the effects of exercise on neuropsychiatric disorders, problem-solving skills, and EI in MS patients.

2. Materials and methods

2.1. Study design / procedure

This study is a prospective cross-sectional study. Ethical approval of the study was given by the Local Ethics Committee (FU-2020/09–12), following the principles of the Declaration of Helsinki. All participants gave written informed consent prior to enrollment. In this study, 36 female relapsing-remitting multiple sclerosis (RRMS) patients who applied to the neurology outpatient clinic of our hospital and met the inclusion criteria among 97 MS patients with a definite diagnosis of MS according to the revised McDonald criteria (Thompson et al., 2018) were included.

Participants completed outcome measures before and after the 12-week exercise program. The exercise program was planned to be three days a week (at least one day apart). Demographic/clinical information of the participants was obtained at baseline, neurological examinations were performed, and graded exercise testing on a bicycle ergometer was performed to determine aerobic capacity. Participants began the program two days after the graded exercise testing. A blinded neurologist did all tests. After the baseline test, the participants were asked not to do any additional exercise outside their routine. Participants completed the same assessments immediately after the 12-week exercise period.

2.2. Eligibility

Inclusion criteria for the study: To be between the ages of 18–45, to have voluntarily consented to participate in the study, to be at least a high school graduate, to be under follow-up with the diagnosis of MS (RRMS) with attacks and remissions, with the Expanded Disability Status Scale (EDSS) between 1 and 3, not having an attack in the last three months, having adequate well-being in following and implementing the exercise program given, not at risk for participation in physical activity (reported as 'yes' to less than two questions on the Physical Activity Readiness Questionnaire [PAR-Q]]), and individuals with doctor approval to exercise.

Participants were excluded if they suffered from acute MS attack or had a history of an attack in the last three months, had been diagnosed with any other known neuromuscular disorder other than MS, had immunomodulatory treatment started in the last six months, and had high spasticity of the extremity (Ashworth Score 3 or 4).

2.3. Data collection tools

Demographic and clinical characteristics: Data on age, education level, EDSS score, marital status, and duration of MS were collected through a questionnaire.

2.3.1. Aerobic capacity

Cardiovascular fitness was included for manipulation control of the ergometer exercise training intervention and prescribing exercise training intensities based on heart rate reserve (HRR). When assessing aerobic capacity, peak oxygen consumption (VO2peak) and maximum heart rate (HRpeak) were measured using an incremental exercise test on an electronically braked and computer-operated bicycle ergometer (Ergoline Ergoselect 200 P, Carefusion Netherlands, Houten, The Netherlands) and a calibrated open-circuit spirometry system (FitMate® Pro, Cosmed).

A 3 min warm-up at 0 W took place prior to the incremental exercise test: The initial run rate for the incremental exercise test was 0 W, and the run rate was continuously increased by 15 W per minute until the participant reached voluntary fatigue (inability to continue exercising) or maximum heart rate. This protocol has been validated in people with MS to measure maximum aerobic capacity (Motl and Fernhall, 2012). HR was monitored using a Polar chest strap (Cosmed®), and HR and degree of perceived exertion were recorded per minute.

2.3.2. Short form-12 version 2 (SF-12v2)

The SF-12v2 is a psychometrically validated, reliable, generic HRQoL instrument that assesses patients' physical and mental health (Foley et al., 2017). It is a short form of the SF-36, which is frequently used in clinical trials. The SF-12v2 consists of 12 questions from the SF-36 that evaluate the exact eight health domains as the SF-36: physical function, the role-physical, bodily pain, general health, vitality, social function, the role-emotional and mental health. The Physical Component Summary (PCS) and Mental Component Summary (MCS) scores are norm-based scores ranging from 0 to 100 calculated from the responses to the 12 questions using scoring software.

2.3.3. Hospital anxiety and depression scale (HAD)

HAD is a scale that screens anxiety and depression symptoms, filled in by the patient him/herself, and is frequently used in the hospital setting. The cut-off point for depression and anxiety subscales is ≥ 8 (Henry et al., 2019).

2.3.4. Modified fatigue impact scale (MFIS)

MFIS is a self-reported fatigue scale commonly used in clinical studies (Rooney et al., 2019). The MFIS includes 21 questions, assessing fatigue's physical, cognitive, and social impacts. The rating was made based on a four-level scale from zero (no problem) to four (severe problem), and a low score indicates a low degree of fatigue.

2.3.5. Problem-Solving inventory (PSI)

In the Likert-type inventory, each item is scored between 1 and 6. Three items are excluded from the scoring. Certain inventory items are reverse-scored. It is assumed that 32 items represent adequate problem-solving skills. A high scale score indicates that the individual considers him/herself inadequate, exhibits avoidance-attachment behavior, and does not feel personal control. The scale scores could range between 32 and 192 (Possa et al., 2017).

2.3.6. Emotional intelligence scale (EIS)

"Emotional Intelligence Assessment Scale" includes five subscales: Emotional awareness (items 1, 2, 4, 17, 19, 25), emotion management (items 3, 7, 8, 10, 18, 30), self-motivation (items 5, 6, 13, 14, 16, 22), empathy (items 9, 11, 20, 21, 23, 28), relationship control (items 12, 15, 24, 26, 27, 29). The 6-point Likert-type scale (1: completely disagree, 2: partially disagree, 3: slightly disagree, 4: slightly agree, 5: partially agree, 6: completely agree) includes 30 items. There are no reverse-scored items. A total score of 155 or higher is considered high (very strong), scores between 130 and 150 are considered normal (some improvement needed), and scores of 129 and below are considered low (definitely needed improvement) emotional intelligence (Ergin, 2000).

2.4. Interventions

The exercise training intervention in MS included the American College of Sports Medicine (ACSM) exercise prescription guidelines, and a 12-week supervised combined exercise program suggesting that a well-characterized strength and aerobic exercise exerts more beneficial effects on cognitive performance (Medicine ACoS, 2013). Exercise training was performed three times a week for 12 weeks and was administered by a trained physical therapist who did not participate in the assessments. This exercise protocol provides an initial phase of warm-up followed by strength training consisting of three exercises for the lower limbs (Squat, Lateral Lunges, and Calf + Leg flexion), and three for the upper limbs (Biceps Curl + Arm Extension and Triceps push), at 50% of one-repetition max (1RM) evaluated after a familiarization phase. Two series of 10 to 12 repetitions were performed for each exercise. The recovery time between the two series was 30–45 s, and the recovery time between different exercises was 1 min. After this stage, aerobic training consisting of 10 min was performed on the bicycle ergometer at 60 - 70% of the maximum aerobic capacity ($VO2_{max}$) (Dalgas et al., 2009). To verify the precision of the aerobic exercise prescription during training sessions, participants were measured continuously using a chest strap transmitter that allowed digital heart rate monitoring. In the last stage of the protocol, stretching exercises of large muscle groups and breathing exercises were performed.

2.5. Statistical analysis

Data were analyzed using SPSS for Windows version 22.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). According to the Skewness and Kurtosis values (between −2 and +2), it was determined that our data did not show a normal distribution. The sample size of 36 patients was based on a power analysis performed in G * Power 3.1 to determine a $\rho \geq 0.40$ correlation from a previous study in MS (Prakash et al., 2010). Alpha value was accepted as 0.05 and beta value as 0.80. Continuous variables were expressed as mean ± standard deviation. The pre-training and post-training values of the parameters were compared using Paired-Samples *t*-test. $P < 0.05$ was considered statistically significant.

3. Results

Table 1 presents the demographic and clinical characteristics of the 36 RRMS patients included in the study. Two patients were excluded from the study since they did not complete the training program. While the mean EDSS of the participants was 1.2 ± 0.46, the mean BMI was 24.42 ± 5.24. The mean duration of MS disease of the patients is 3,08±1,35 (Table 1). Six of the patients used interferon β−1a 3 times a week, five of the patients used glatiramer acetate, 14 used fingolimod, 6 used dimethyl fumarate, and 3 of them used ocrelizumab. Twenty-three of the participants were high school graduates, and eleven of the participants were university graduates.

The patients' data before and after the 12-week exercise program session are given in Table 2.

While a significant increase was observed in the HRpeak values of the participants after the exercise ($p < 0.05$), the $VO2_{max}$ values also showed a highly significant difference compared to the pre-treatment ($p < 0.01$). While a significant difference was found in the mental subparameter of SF-12 in the treatment ($p < 0.05$), a high level of significant difference was found in the physical subparameter ($p < 0.01$). While no significant difference was observed in the HAD anxiety subparameter ($p > 0.05$), a significant difference was found in the depression subparameter ($p < 0.01$). There was a significant difference in MFIS physical and cognitive subparameters compared to pre-treatment ($p < 0.01$). A significant difference was observed in the EIS total score after the treatment ($p < 0.01$). As a result, significant differences in all scales were in the direction of the well-being of the participants (Table 2).

4. Discussion

This study aimed to examine the effects of physical exercise on problem-solving skills, emotional intelligence, and neuropsychiatric conditions in mild disabled RRMS patients. In addition, studies evaluating treatments and/or interventions that reduce cognitive impairment in MS patients are lacking in the literature. This pilot study aimed to develop a short combined exercise program with multi-targeted therapeutic potential by focusing on problem-solving skills and emotional intelligence problems in MS patients. Our findings showed that a 12-

Table 1
Demographic and clinical characteristics of patients.

	X ± SD	min	max
Age (Years)	30.31 ± 5.60	21	44
EDSS	1.69 ± 0.49	1	2.5
BMI (kg/m2)	24.42 ± 5.24	18	37.1
MS disease duration (Years)	3,08 ± 1,35	1	6

X: Mean, SD: Standart Deviation, BMI: Body mass index, Continuous variables are presented as mean ± standard deviation (SD), EDSS: *Expanded Disability Status Scale.*

Table 2
Aerobic capacity before and after exercise, neuropsychiatric inventory data, emotional intelligence levels, and problem-solving skills.

		Pre-training $X \pm$ SD	Post-training X±SD	t	p-value
HR_{peak}		15,278 ± 7,08	15,493 ± 6,25	−2363	0,025*
VO_{2max} (ml/kg/min)		1986 ± 3,52	2072 ± 3,39	−3517	0,001**
SF-12v2	***Physical***	4125 ± 2,70	4256 ± 2,90	−3219	0,003**
	Mental	3509 ± 2,35	3597 ± 3,48	−2403	0,022*
HAD	***Anxiety***	619 ± 1,33	609 ± 1,03	0,649	0,521
	Depression	969 ± 2,86	878 ± 2,21	2873	0,007**
MFIS	***Physical***	1862 ± 5,16	1713 ± 4,93	3115	0,004**
	Cognitive	1775 ± 3,89	1613 ± 3,63	4762	0,000**
EIS Total		9803 ± 18,68	10,178 ± 16,99	−2749	0,010*
PSI		12,038 ± 13,44	11,609 ± 11,27	2859	0,008**

X: Mean, SD: Standart Deviation, HR_{peak}: Maximum heart rate, VO_{2max}: Maximum aerobic capacity, SF-12v2: Short Form-12 Version 2, HAD: Hospital Anxiety and Depression Scale, MFIS: Modified Fatigue Impact Scale, EIS: Emotional Intelligence Assessment Scale, PSI: Problem-solving Inventory,.

* $p < 0.05$,.

** $p < 0.01$.

week combined exercise program significantly increased problem-solving skills and emotional intelligence levels and improved neuropsychiatric conditions.

Physical inactivity may be associated with the development of some mental disorders. In some clinical and epidemiological studies, it has been shown that there is a cross-sectional and prospective relationship between depression and anxiety symptoms and physical activity (Canan and Ataoğlu, 2010). In the study conducted by Canan et al., it was found that the symptoms of depression and anxiety decreased as the time spent doing sports increased in the individuals participating in the study (Canan and Ataoğlu, 2010). In another study, physical activity was positively associated with increased general mood scores while negatively associated with depressive symptoms, anxiety scores, hostility, and psychotic behaviors (Szabo and Urbán, 2014). In parallel with these findings, our study showed that physical activity caused a significant decrease in HAD depression data and problem-solving skills, but contrary to the literature findings, it did not cause a significant decrease in the anxiety subgroup.

In our study, a significant improvement was observed in fatigue and quality of life measures, and depression. MS can reduce the quality of life, and although the reduced quality of life is partly due to physical disability, it is also affected by depression, neuropsychiatric disorder, and cognitive dysfunction (Barry et al., 2018). Current results have shown that regular exercise can improve the quality of life of MS patients. Pazokian et al. showed that regular exercise is very beneficial for MS patients. In this study, regular exercise improved muscle cramps, increased flexibility, and reduced fatigue in these patients (Pazokian et al., 2013). Similar to the studies in the literature, we think that these improvements in quality of life are secondary results of the exercise. In fact, in previous studies, combined exercise training showed moderate to advanced improvements in walking capacity, all dimensions of fatigue, and both physical and mental quality of life (Barry et al., 2018; Gonzales et al., 2017). It is impossible to determine whether our combined exercise protocol resulted in a more significant change, as the outcome measures vary. Proinflammatory cytokines can affect neuronal and neuroendocrine functions and induce behavioral symptoms, including fatigue, anxiety, depression, withdrawal from social activities, and cognitive deficits called illness behavior (Dantzer and Kelley, 2007). We think these significant improvements in our participants ameliorated pathologies by activating a series of immunological and hormonal responses with exercise (Rossi et al., 2009; Ormstad et al., 2020).

Perception, understanding, and regulation of emotions are important factors of emotional intelligence that affect the social, emotional, and behavioral aspects (Ghajarzadeh et al., 2014). Emotional Intelligence (EI) is an important indicator of health. In different studies, it has been observed that an increase in physical activity causes an increase in stress management skills, which increases the ability to manage, regulate, and control emotions and results in higher EI scores (Gabour, 2020). Several researchers have studied the relationship between physical activity and EI. Some of these studies are case-control studies, some are experimental designs, and most are observational studies. The common finding of these studies is that physical activity causes high EI scores (Gabour, 2020; Ruiz-Ariza et al., 2018; Zysberg and Hemmel, 2018). In the study of Gabaur, it was determined that adolescents who exercise for 1–2 h daily have higher EI scores than adolescents who exercise less than 30 min; that is, the EI score increases in direct proportion with the increase in the duration of regular physical activity (Gabour, 2020). Although there is no study examining the effect of physical activity on emotional intelligence in MS patients, there is also evidence in studies conducted in MS animal models that exercise may be protective against neurodegenerative synaptic and dendritic changes caused by inflammation in the nervous system (Rossi et al., 2009). However, some reports have been reported in the literature that emotional intelligence improves physical performance in MS patients. In a study conducted by Mehrabi et al. in 70 patients with MS, it was reported that emotional intelligence training improved self-efficacy scores in patients (Mehrabi et al., 2017). As our results showed, exercise in RRMS patients produced significant improvements in EI, indicating that exercise affects emotional well-being and regulation in RRMS. It is not surprising that EI plays a role in many different areas of life and improves other neuropsychiatric parameters. These findings are consistent with the literature on physical activity increasing EI scores and reducing psychiatric symptoms in different patient groups without MS. In the literature, we could not find any study investigating the effects of exercise on EI in MS patients. For this reason, our study is a pioneering study for future studies to investigate the positive effects of this non-pharmacological exercise application in detail.

Interestingly, no studies are investigating the effect of physical exercise on problem-solving skills in MS patients. Although the positive effects of physical activity on cognitive functions have been shown, its effect on problem-solving skills is not known. Increased habitual physical activity is associated with making quick and independent decisions and increasing problem-solving skills (Canan and Ataoğlu, 2010; Kolpakov et al., 2017). Solving problems is an integral part of EI (Lane et al., 2010). In addition, a study reported that emotional intelligence and cognitive disorder are directly related. As cognitive disorder increases, it has been shown that emotional intelligence level decreases (Owji et al., 2018). It is believed that individuals with high EI scores cope with stress more effectively, and exercise is a positive mood stabilizer (Lane et al., 2010). In the studies conducted by Laborde et al., it was shown that athletes with high EI scores could cope with stress more (Laborde et al., 2015, 2012). Eminoğlu Tek et al. reported that physical activity improves cognitive functions such as memory, perception, attention, language, visuospatial functions, and quality of life in elderly individuals (Eminoğlu, 2019). In the study of Veziroğlu, it was concluded that while doing sports in secondary school students affected the reflection subdimension in problem-solving skills; it did not affect the other subdimensions (Veziroğlu et al., 2020). In different studies comparing those who do sports and those who do not, it has been found that those who do sports are more lively, extroverted, hardworking, more patient, more ready to establish social relations, and adapt to a new environment more quickly. It has been determined that those who do sports are more emotionally balanced than those who do not (Veziroğlu et al., 2020; Tiryaki et al., 1991; Eliöz et al., 2019). According to our findings, it was found that exercise increases problem-solving skills. We think that the possible mechanisms in this improvement may be due to increased neurotrophin levels, reduction in systemic inflammation, and defective protein accumulation, known as the effect of exercise. In addition, the fact that exercise increased the EI score may have contributed positively to problem-solving skills. MS patients with poor problem-solving skills may experience frequent adverse outcomes that lead to expectations of failure and chronic anxiety. This fear of failure may hinder MS patients' engagement in previously enjoyable activities. The resulting isolation can lead to more anxiety and increased fear of failure. The strong relationship between anxiety and problem-solving abilities should be further explored with additional executive function tests emphasizing planning and set-shifting abilities.

Our study has several limitations. The limitations of this study were that only female RRMS patients were included in our study and that all participants had an EDSS score of less than 4.5. Therefore, it is recommended that future studies be conducted on both men and women in different types of MS with higher EDSS scores. Furthermore, our study is strictly preliminary and is limited by a few factors, such as the relative heterogeneity of the participants.

5. Conclusion

Few studies evaluate treatments and/or interventions that reduce cognitive impairment in MS patients. We designed this study to evaluate how exercise affects EI and problem-solving skills in MS patients. While our design cannot provide a comprehensive explanation of how exercise relates to neuropsychological, EI, and PSI in individuals with MS, it does add to a growing body of data revealing its effects on physical and mental (especially emotional) health. Future research should explore how exercise can alleviate EI, PSI, and neuropsychiatric conditions in MS and how these affect neurophysiological mechanisms.

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Compliance with ethical standards

Ethical approval our study was approved according to the local ethical committee. All patients gave informed written consent to be enrolled in the study according to the Declaration of Helsinki.

CRediT authorship contribution statement

Irem Tasci: Methodology, Writing – original draft, Writing – review & editing, Investigation. **Caner Feyzi Demir:** Conceptualization, Writing – original draft, Visualization. **Furkan Bilek:** Validation, Investigation, Resources, Writing – review & editing. **Sait Albayrak:** Investigation, Resources.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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