

ORIGINAL ARTICLE

Does remission in rheumatoid arthritis bring kinesiophobia, quality of life, fatigue, and physical activity closer to normal?

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ABSTRACT

Objectives: This study aimed to compare kinesiophobia, fatigue, physical activity, and quality of life (QoL) between the patients with rheumatoid arthritis (RA) in remission and a healthy population.

Patients and methods: The prospective controlled study included 45 female patients (mean age: 54.22 ± 8.2 year; range, 37 to 67 year) with a diagnosis of RA determined to be in remission according to the Disease Activity Score in 28 Joints (DAS28) being ≤ 2.6 between January 2022 and February 2022. As a control group, 45 female healthy volunteers (mean age: 52.2 ± 8.2 year; range, 34 to 70 year) of similar age were evaluated. The QoL, disease activity, pain, kinesiophobia, fatigue severity, and physical activity were assessed using the Health Assessment Questionnaire, DAS28, Visual Analog Scale, Tampa Scale of Kinesiophobia, Fatigue Severity Scale, and International Physical Activity Questionnaire, respectively.

Results: There was no significant difference between the groups in demographic data. A statistically significant difference was found between the groups in terms of pain, C-reactive protein level, fatigue, kinesiophobia, QoL, and total, high, and moderate physical activity scores (p<0.001). Among the RA patients in remission, there was a significant correlation between kinesiophobia and moderate physical activity and QoL, as well as between fatigue and high physical activity (p<0.05).

Conclusion: Patient education and multidisciplinary approach strategies should be developed to increase the QoL and physical activity and reduce kinesiophobia in RA patients in remission since there may be a decrease in physical activity due to kinesiophobia, fatigue, and fear of movement in this patient group compared to the healthy population, impairing their QoL.

Keywords: Kinesiophobia, remission, rheumatoid arthritis, pain, physical activity.

Rheumatoid arthritis (RA) is a multisystemic, chronic, progressive autoimmune disease characterized by the inflammation of synovial joints and tendon sheaths and has both genetic and environmental factors in its etiology.^{1,2} RA is the most common inflammatory joint disease, affecting 1% of the global population.³ The disease most commonly begins in the 40s and 50s. It is three times more common in females, and 80% of patients are aged between 35 and 50 years.^{1,4} Rheumatoid arthritis manifests with symmetrical polyarticular involvement, primarily in the hand, elbow, knee, ankle, and shoulder joints.⁵ Pain, swelling, and tenderness increase with movement in the affected joint, and stiffness is often observed.⁶ Painful joints and fatigue are often accompanied by morning stiffness lasting more than half an hour.⁷ In addition to complaints related to the joints, 50% of patients with RA also develop systemic extra-articular findings at any time during the disease.⁸ The main goal in the treatment of RA is to reduce disease

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activity, joint damage, and functional loss.⁹ In recent years, the growing popularity of biologic agents and disease-modifying antirheumatic drugs (DMARDs) and their frequent use in RA treatment have led to increased success in treatment.¹⁰ Remission refers to the disappearance of the symptoms and markers of the disease, but this does not mean complete recovery.¹¹ Remission is the result of a successful treatment process in which the patient's joint and extra-articular inflammation is suppressed. The clinical decision for remission is primarily based on inflammation symptoms, functional disability, and joint damage, but laboratory findings and evaluation also play a role in this process.^{9,11}

There are different criteria available to decide on a patient's remission status, including those described by the American College of Rheumatology (ACR), European Alliance of Rheumatology Associations for (EULAR), International League of Associations for Rheumatology (ILAR), and the US Food and Drug Administration. The Disease Activity Score in 28 Joints (DAS28), one of the most commonly used remission measures, evaluates the remission status of the disease according to EULAR. Although ankle and foot joints are excluded from assessment in DAS28, it can be used in the routine follow-up of disease activity as it is more practical to calculate. DAS28 involves the evaluation of a total of 28 joints in terms of the number of tender and swollen joints, the general health status of the patient, and acute phase reactants, and patients with a score ≤ 2.6 are considered in remission.¹⁰

Kinesiophobia is a type of fear-avoidance behavior defined as the excessive fear of physical activity and movement and develops in the presence of persistent pain as a result of painful injury and sensitivity to reinjury.¹² Pain and fear are interrelated, and pain can cause physical, behavioral, and cognitive fear responses in patients.^{13,14}

In RA, arthritis and joint pain can cause kinesiophobia, and patients with chronic pain tend to avoid movement, believing that pain may increase with physical activity and lead to a risk of injury. This can result in reduced mobility, muscle strength, and aerobic capacity. In addition to these physiological changes in patients, kinesiophobia can cause psychosocial changes, depression, and anxiety. All these conditions lead to a decrease in the patient's quality of life (QoL).^{15,16} Fatigue is another common symptom seen in patients with RA. Although the etiology of fatigue is unknown, it is associated with chronic pain, limitation, inflammation, and psychosocial factors and may affect the patient's functionality and QoL.¹⁷

To the best of our knowledge, the literature contains no study on kinesiophobia, fatigue, physical activity, and life quality in patients with RA that are in remission. Therefore, the aim of our study was to reveal whether there was any difference in kinesiophobia, fatigue, physical activity, and QoL of patients with RA in remission compared to a healthy population.

PATIENTS AND METHODS

The prospective controlled study included 45 female patients (mean age: 54.22±8.2 year; range, 37 to 67 year) who presented to the Physical Medicine and Rehabilitation Outpatient Clinic of the Kütahya Health Sciences University Hospital between January 2022 and February 2022 with a diagnosis of RA and were determined to be in remission based on DAS28 being ≤ 2.6 . Forty-five female healthy volunteers (mean age: 52.2±8.2 year; range, 34 to 70 year) were recruited for the study. The RA diagnosis of the patients met the 2010 ACR criteria,18 and their remission times were recorded. Inclusion criteria were as follows: (i) having been diagnosed with RA according to the ACR criteria and being in remission according to the EULAR criteria; (ii) being aged 18-70 years; (iii) volunteering to participate in the study. Exclusion criteria were as follows: (i) being illiterate; (ii) having a neuromuscular disease; (iii) having difficulty walking; (iv) having a cognitive disorder; (v) being unable to cooperate; (vi) being followed up due to any psychiatric disorder.

Demographic and clinical evaluation

The demographic data of the patients were recorded, and their physical examination was performed. Age, height, weight, body mass index, disease duration, and medications used were also questioned. During the physical examination, the affected joints of the patients were evaluated. Life quality of the patients was assessed using the Health Assessment Questionnaire (HAQ). Disease activity was evaluated using DAS28, and pain levels were determined using the Visual Analog Scale (VAS). Kinesiophobia, fatigue severity, and physical activity were assessed using the Tampa Scale of Kinesiophobia (TSK), Fatigue Severity Scale (FSS), and the International Physical Activity Questionnaire (IPAQ), respectively. Individuals in the healthy control group were also evaluated using the TSK, FSS, HAQ, and IPAQ.

Evaluation parameters

Visual Analog Scale

The pain levels were evaluated using the VAS. The patients were asked to consider the severity of pain they felt within the last week and mark it on a 10-cm line, where one end represents the best disease period and the other indicates the worst. The marked point was measured in centimeters (0-10 cm).¹⁹

Disease Activity Score in 28 Joints

Disease activity was assessed with DAS28, which was calculated using the number of tender and swollen joints, patient global assessment (VAS 0-10 cm), and acute phase reactants. DAS28 \leq 2.6 was regarded as remission, 2.6-3.2 as low disease activity, 3.3-5.1 as moderate disease activity, and >5.1 as high disease activity.^{20,21}

Health Assessment Questionnaire

The general health status of the patients was evaluated with HAQ, which examines the activities of daily living under eight sections (dressing, self-care activities, arising, eating, walking, hygiene, reaching, and grip). Each item is scored between 0 and 3 points. If the patient could not perform the activity stated in the item, that item was scored 0, and it was scored 3 if they could easily manage the task.²² The validity and reliability studies of the Turkish version of HAQ were undertaken by Küçükdeveci et al.²³

Tampa Scale for Kinesiophobia

TSK was used to evaluate kinesiophobia. This is a 17-item scale developed to measure fear of movement/reinjury. The scale includes parameters of injury/reinjury and fear-avoidance behavior in work-related activities based on a 4-point Likert scale (1=strongly disagree, 4=strongly agree). After reversing items 4, 8, 12, and 16, a total score is calculated. The total score ranges from 17 to 68, with a high score indicating a high level of kinesiophobia.²⁴ The validity and reliability of the Turkish version of TSK were reported by Tunca Yılmaz et al.²⁴

Fatigue Severity Scale

FSS was used to evaluate the severity of fatigue experienced by the patients within the last week. The scale consists of nine statements, of which participants score from 0 (completely disagree) to 7 (completely agree). Accordingly, a score <2.8 is considered to indicate no fatigue, while scores >6.1 indicate chronic fatigue syndrome. Gencay-Can and Can²⁵ performed the validity and reliability analyses of the Turkish version of FSS.

International Physical Activity Questionnaire

Physical activity status was assessed using IPAO, which questions whether an individual has engaged in physical activity within the last week, and if they have, at what intensity and frequency. In IPAQ, the criterion for any physical activity is a duration of at least 10 min at a time. The durations of high physical activities (e.g., football, basketball, aerobics, fast cycling, weight lifting, and carrying loads), moderate physical activities (e.g., carrying a light load, cycling at normal speed, folk dance, dancing, bowling, and table tennis), walking, and sitting are calculated in minutes and converted to the metabolic equivalent (MET) corresponding to the basal metabolic rate to obtain the total physical activity score (MET-min/week). According to the total physical activity score, the physical activity levels of the participants are classified as low (600 MET-min/week), moderate (600-3,000 MET-min/week), and high (above 3,000 MET-min/week). Ozturk²⁶ reported the validity and reliability of the Turkish version of IPAQ.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 24.0 software (IBM Corp., Armonk, NY, USA) Frequency tables and descriptive statistics were used to interpret the findings. The conformity of the variables to the normal distribution was examined with visual

		Rheı	Rheumatoid arthritis group (n=45)	is group (n=	45)			Control group (n=45)	ıp (n=45)			
	ц	%	Mean±SD	Median	Min-Max	Ľ	%	Mean±SD	Median	Min-Max	t, z, χ^2	d
Age (year)			54.22±8.2	54	37-67			52.2±8.2	54	34-70	1.146	0.255
Body mass index (kg/m^2)			31.2 ± 6.7	30.30	21.50-47.70			31.4±7.5	31.50	21-47.70	-0.127	0.899
Occupation Retired Housewife Physical worker Desk worker	4 6 ³³ 2	4.4 73.3 13.3 8.9				0 2 0	0 88.9 11.1 0				6.762	0.080
Education level Illiterate Literate Primary school Middle school High school University	6 Ю О О О I I I 0 О О О О О О	28.9 22.2 0.2 11.1 4.4 13.3				30 2 5 17 8	0 37.8 11.1 4.4 0 6.7				8.050	0.154
Smoking status Smoker Non-smoker	2 43	4.4 95.6				00	8.9 91.1				0.714	0.398
Chronic disease Asthma DM HT HT+DM HT+COPD+DM Cardiac disease COPD Thyroid disease None	2 - 2 - 4 - 2 - 2	0 4.4 2.2 8.9 8.9 2.2 2.2 64.4				$^{32}_{32}$ 32	6.7 0 0 2.2 2.2 6.7 6.7 71.1				9.576	0.296

(histogram and probability graphs) and analytical (Shapiro-Wilk test) methods. The Mann-Whitney U test was used to analyze nonnormally distributed parameters, the independent samples t-test for normally distributed parameters, and the chi-square test for the comparison of two qualitative values. The relationship between normally distributed data was analyzed using the Pearson correlation test, and the relationship between nonnormally distributed data was analyzed with the Spearman correlation analysis. In all statistical analyses, the significance level was accepted as a p value <0.05. According to the power analysis calculation, with a 5% alpha margin of error and 80% power, the sample size was calculated as 30 patients for each group, for a total of 60 participants.

RESULTS

The demographic characteristics of the participants were given in Table 1. There was no statistical difference between the two groups in terms of age, body mass index, occupation, education level, smoking, and chronic diseases (p=0.255, p=0.899, p=0.080, p=0.154, p=0.398, and p=0.296, respectively). The number of patients who used drugs for RA treatment (biological agents, DMARDs, steroids, and their combinations), rheumatoid factor positivity status, presence of morning stiffness, joint involvement, duration of remission (days), and DAS28 scores are presented in Table 2.

There were statistically significant differences in VAS scores (p<0.001), C-reactive protein (CRP) values (p<0.001), FSS scores (p<0.001), TSK scores (p=0.004), HAQ scores (p<0.001), IPAQ high scores (p=0.001), IPAQ moderate scores (p=0.054), and IPAQ total scores (p=0.046) between the groups as shown in Table 3. Only the walking and sitting subparameters of IPAQ were found to be similar in both groups (p=0.667 and p=0.848, respectively; Table 3).

In the RA group, the IPAQ-high score had a statistically significant correlation with the TSK score (p=0.002) and FSS score (p=0.038). In addition, a statistically significant correlation was observed between the IPAQ moderate score and the IPAQ high score (p=0.008) and TSK scores (p=0.019). There was a statistically

			Patients with RA	(n=45)	
	n	%	Mean±SD	Median	Min-Max
Duration of remission (day)			167.4±112.5	120	0-480
DAS28			2.0 ± 0.5	2.11	0-2.33
RA treatment					
Biological agent	1	2.2			
DMARD	19	42.2			
DMARD, biological agent	3	6.7			
No medication	4	8.9			
Steroid	4	8.9			
Steroid + DMARD	14	31.1			
Rheumatoid factor					
Negative	11	24.4			
Positive	34	75.6			
Morning stiffness					
Present	2	4.4			
Absent	43	96			
Joint involvement					
Single joint	21	46.6			
None	24	53.4			

RA: Rheumatoid arthritis; SD: Standard deviation; DAS28: Disease Activity Score in 28 joint; DMARD: Disease-modifying anti-rheumatic drug.

	Rheumatoid ar	thritis grou	o (n=45)	Control	group (n=4	5)		
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	t, z	р
VAS	2.4±1.7	2	0-7	0.9 ± 1.2	0	0-4	-4.709	< 0.001
CRP	6.0±3.9	6	0-13.80	3.4±1.3	3	1-7	-3.631	< 0.001
FSS score	5.1±2	5.88	1.10-7	2.1±1.9	1.88	0-6.66	-5.961	< 0.001
TSK score	38.5±15.7	41	17-68	29.6±11.2	29	0-47	-2.8617822	0.004
HAQ score	1.8 ± 0.6	2	0-3	0.3±0.5	0	0-1.33	-7.777	< 0.001
IPAQ-high	136.0±189.9	0	0-480	354.7±318.7	320	0-960	-3.337	0.001
IPAQ-moderate	205.3±192.2	180	0-960	335.1±324.3	180	0-1680	-1.93	0.054
IPAQ-walking	511.8±254.8	495	0-1386	668.8±654.8	495	0-2772	-0.43	0.667
IPAQ-sitting	1127.6±1085.6	600	300-4200	1062.2±104	600	300-4200	-0.192	0.848
IPAQ-total	1980.7±1104.8	1674	700-5020	2420.8±1271.8	2120	360-5600	-1.997	0.046

SD: Standard deviation; VAS: Visual analog scale; CRP: C-reactive protein; FSS: Fatigue Severity Scale; TSK: Tampa Scale of Kinesiophobia; HAQ: Health Assessment Questionnaire; IPAQ: International Physical Activity Questionnaire; t: independent samples t-test statistic; z: Mann-Whitney U test.

significant correlation between the IPAQ sitting score and the IPAQ total score (p<0.001). The TSK score statistically significantly correlated with the IPAQ high score (p=0.002), IPAQ moderate score (p=0.019), and the QoL score (p=0.019, Table 4).

DISCUSSION

In this study, a statistically significant relationship was found between the patients with RA in remission and healthy controls in terms of pain, CRP values, fatigue, kinesiophobia, QoL, and high and moderate physical activity, while there was no significant relationship between VAS scores and other parameters within the RA group. A significant relationship was detected between high physical activity and kinesiophobia and fatigue, as well as a significant relationship between kinesiophobia and QoL.

In the literature, in one of the studies evaluating pain in patients with RA in remission using different remission criteria, patients were followed up for one year according to the DAS28 and CRP or ACR/EULAR remission criteria, and it was determined that clinically significant pain continued in remission identified based on DAS28 but not according to the ACR/EULAR criteria.²⁷ For the DAS28 remission group, patient global assessment, disability, fatigue, sleep problems, and self-efficacy were strongly associated with pain severity at baseline and one year, whereas inflammatory disease activity and joint damage were not significantly associated with elevated pain severity at either evaluation period. This may have been due to the differences between the DAS28 and ACR/EULAR remission criteria and patients with a patient global assessment score ≥ 2 and a CRP value >2 mg/dL considered not in remission according to the latter.

Previous research has shown that many patients with RA continue to experience fatigue even after achieving remission or low disease activity.²⁸ In a study examining fatigue in patients with RA in remission or with low disease activity over a six-month follow-up, 27.9% of patients had a fatigue VAS score ≥ 40 mm, and lower erythrocyte sedimentation rate (ESR) and higher pain at baseline were determined to be statistically significant predictors of higher levels of fatigue, while younger age and greater pain were significantly associated with higher levels of fatigue at six months. The authors suggested that there was a need for a mechanism to cope with pain.²⁹ In the current study, the FSS score was found to be significantly higher in patients with RA in remission than in healthy controls, but

no relationship was found between fatigue, pain, and CRP in RA patients in remission. Therefore, we consider that further studies are needed to evaluate factors affecting fatigue in detail.

Kinesiophobia had previously not been evaluated in studies of RA in remission, but there are studies evaluating this condition in patients with RA. Baysalhan Öztürk et al.³⁰ stated that the rate of kinesiophobia was 70%, and kinesiophobia in RA was positively associated with the total number of swollen and tender joints, DAS28, pain, and QoL scores and negatively associated with quadriceps muscle strength and knee flexion. The authors also reported a correlation between kinesiophobia scores and fatigue. In another study examining the relationship between QoL and kinesiophobia in 88 patients with RA and 93 healthy volunteers, kinesiophobia was found to be significantly higher in the RA group compared to the control group, and fatigue scores were stated to be one of the independent variables affecting kinesiophobia.³¹ In other studies conducted with patients with RA, Lööf et al.¹⁵ and Kınıklı et al.³² demonstrated that high pain levels were associated with an increased risk of high fear-avoidance behavior or kinesiophobia. In our study, no relationship was found between pain and kinesiophobia in patients with RA in remission, which may have been due to the low pain scores of the patients.

In a study examining possible predictors of remission and normalized physical function in patients with RA in remission over a one-year follow-up, DAS28, HAQ, pain, and fatigue scores of patients in remission were lower throughout the year and similar at baseline compared to patients not in remission.³³ Similarly, in a study examining QoL, the scores of the disability index of HAQ were reported to be higher in low disease activity compared to the remission group at the six- and 12-month follow-ups.³⁴ In the current study, the QoL scores were lower in the RA patients in remission compared to the controls, and a relationship was found between QoL and kinesiophobia. Therefore, we suggest that it is necessary to develop strategies to eliminate kinesiophobia and increase the QoL in this patient population.

In terms of physical activity, there are studies showing that physical activity decreases in patients

Table 4. The relationship between physical activity, kinesiophobia, fatigue, and quality of life	elationship	between	n physical	activity,	kinesioph	lobia, fat	igue, and	l quality c	of life							
	IPAQ (n=	IPAQ-High (n=45)	IPAQ-Moderate (n=45)	oderate 45)	IPAQ-Walking (n=45)	Valking 45)	IPAQ-Sitti (n=45)	IPAQ-Sitting (n=45)	IPAQ-Total (n=45)	-Total 45)	TSK Score (n=45)	Score 45)	FSS Score (n=45)	icore 15)	HAQ Score (n=45)	Score 45)
	r	d	r	d	r	d	r	d	г	d	r	d	r	d	r	d
VAS	-0.403	0.234	0.234	0.122	0.102	0.505	-0.124	0.419	0.084	0.582	0.211	0.164	0.236	0.118	-0.024	0.876
IPAQ-High	1	I	0.388^{**}	0.008	-00.0	0.955	-0.03	0.844	0.272	0.07	0.453	0.002	-0.134	0.038	-0.202	0.183
IPAQ-Moderate	0.388	0.008	1	I	0.157	0.303	-0.061	0.689	0.282	0.061	0.348	0.019	0.002	0.991	0.062	0.686
IPAQ-Walking	-00.00	0.955	0.157	0.303	1	ı	-0.061	0.692	0.201	0.185	0.021	0.892	-0.212	0.161	0.091	0.551
IPA-Sitting	-0.03	0.844	-0.061	0.689	-0.061	0.692	1	ı	0.814	<0.001	-0.052	0.732	0.143	0.35	0.18	0.236
IPAQ-Total	0.272	0.07	0.282	0.061	0.201	0.185	0.814	<0.001	1	ı	0.152	0.326	0.135	0.376	0.209	0.169
TSK	0.453	0.002	0.348	0.19	0.021	0.892	-0.052	0.732	0.15	0.326	1	ı	0.134	0.39	-0.348	0.019
FSS	-0.134	0.038	0.002	0.991	-0.212	0.161	0.143	0.35	0.135	0.376	0.134	0.379	1	,	-0.204	0.178
HAQ	-0.202	0.183	0.062	0.686	0.091	0.551	0.18	0.236	0.209	0.169	-0.348	0.019	-0.204	0.178	1	ŀ
IPAQ: International Physical Activity Questionnaire; VAS: Visual	hysical Activit	y Questionr.	naire; VAS: V	'isual Analoç	Analog Scale; TSK: Tampa Scale of Kinesiophobia; FSS: Fatigue Severity Scale; HAQ: Health Assessment Questionnaire; r: Correlation coefficient.	i: Tampa Sc	ale of Kines	iophobia; FS	SS: Fatigue \$	Severity Scal	le; HAQ: H	ealth Assess	ment Questi	onnaire; r: (Correlation c	oefficient.

with RA compared to the general population,¹⁶ as well as those indicating that physical activity is higher in patients in remission compared to those with low disease activity.³⁵ In our study, the physical activity subparameters were affected by vigorous and moderate physical activity compared to the healthy controls, and vigorous physical activity was correlated with kinesiophobia and fatigue, while moderate physical activity was correlated with kinesiophobia. It can be concluded that approaches targeting fatigue and kinesiophobia should be used to increase the recovery of physical activity in these patients.

To achieve remission in patients with RA. conventional synthetic DMARDs (methotrexate, hydroxychloroguine, and sulfadiazine), targeted synthetic DMARDs (pan-JAK and JAK1/2 inhibitors), and biological DMARDs [tumor necrosis factor (TNF)- α inhibitors, TNF-receptor inhibitors, interleukin (IL)-6 inhibitors, IL-6R inhibitors, B cell depleting antibodies, and inhibitors of costimulatory molecules] are used.³⁶ Drugs used in the treatment of RA greatly improve symptoms and prevent disease progression in patients; however, they also have side effects such as fatigue.³⁷⁻³⁹ In addition, glucocorticoids have been described to have severe multisystemic metabolic and musculoskeletal side effects.^{40,41} Since we used different drug combinations in patients with RA in remission, this may have had an effect on the results being different from the health controls considering the different side effect profiles of the single or combined use of such drugs. In light of our results, we consider that there is a need to detect the differences between RA patients in remission and the healthy population and evaluate these patients in terms of previous joint damage, ongoing psychological problems, and medications, despite them being in remission.

The limitations of this study can be considered the absence of the evaluation of psychological dimension, disease duration before the diagnosis of remission, involved joints, or related markers of joint destruction.

In conclusion, differences were found between RA patients in remission and healthy controls in terms of pain, CRP values, fatigue, kinesiophobia, QoL, and vigorous and moderate physical activity. Kinesiophobia was determined to have a relationship with vigorous and Arch Rheumatol

moderate physical activity and QoL, and fatigue was associated with vigorous physical activity. According to these results, it should be kept in mind that in the follow-up of RA patients in remission, fatigue, lack of physical activity, and deterioration in QoL may occur due to previous joint damage, ongoing psychological problems, and medications used. Patient education and multidisciplinary approach strategies should be developed to increase the QoL and physical activity and reduce kinesiophobia in RA patients in remission.

Ethics Committee Approval: The study protocol was approved by the Kütahya Health Sciences University Clinical Research Ethics Committee (date: 11.01.2022, no: 2022-01/06). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept: A.Ö.; Design, control/supervision, data collection and/or processing, analysis and/or interpretation, writing the article, critical review, references and fundings, materials: A.Ö., M.A.L.; Literature review: A.Ö.

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