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The evaluation of dynamic and static balance in Familial Mediterranean fever patients

Ailevi Akdeniz ateşi hastalarında statik ve dinamik denge bozukluklarının değerlendirilmesi

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Abstract

Objective: Familial Mediterranean fever (FMF) presents with arthritis attacks, enthesitis, and synovitis in the lower extremities which suggests that balance disorders may develop. The purpose of this study is to evaluate the dynamic and static balance in FMF patients.

Methods: This study was a prospective case-control study. The study included FMF patients who met the modified Tel Hashomer criteria as well as healthy participants. FMF patients' demographics, clinical features, International Severity Scoring System and Maastricht Ankylosing Spondylitis Enthesitis score were assessed. The Berg Balance scale (BBS), Functional Reach test (FRT), timed up and go (TUG), and single leg stance (SLS) tests were used to assess balance performance.

Results: The patient group consisted of 94 FMF patients (62.8% females), and the control group consisted of 90 healthy individuals (52.7% females). When the FRT, BBS, TUG, and SLS scores of the patient and control groups were compared, the patient group performed statistically worse in all scores. High risk of fall was found to be associated with longer disease duration and older age ($p<0.001$ and $p<0.001$). Visual analog scale scores during the attack were higher in patients at risk of falling, and arthralgia and amyloidosis were also more common. ($p=0.032$, $p=0.002$, and $p=0.001$, respectively).

Conclusion: The study found that compared to healthy individuals, FMF patients exhibited worse dynamic and static balance. The existence of amyloidosis and enthesitis, together with a longer and more severe illness, could all be factors in balance loss.

Keywords: Dynamic balance, Familial Mediterranean fever, static balance

Öz

Amaç: Ailevi Akdeniz ateşinin (AAA) yaşam boyu süren enflamasyonun yanı sıra alt ekstremitelerde artrit, sinovit ve entezit atakları ile seyretmesi hastalarda denge bozukluğu gelişebileceğini düşündürmektedir. Bu çalışmanın amacı AAA hastalarında statik ve dinamik denge bozukluğunu değerlendirmektir.

Yöntem: Çalışma prospektif olarak dizayn edilen bir çalışmadır. Modifiye Tel Hashomer kriterlerini karşılayan AAA hastaları ve sağlıklı gönüllüler çalışmaya dahil edildi. AAA hastalarının demografik verileri, klinik özellikleri, Maastricht Ankilozan Spondilit Entezit Skoru ve Uluslararası Şiddet Skorlama Sistemi değerlendirildi. Denge performansı Berg Denge ölçeği (BBS), fonksiyonel uzanma testi (FRT), zamanlı kalk ve yürü (TUG) ve tek ayak duruşu (SLS) testleri ile değerlendirildi.

Bulgular: Hasta grubuna 94 AAA hastası (%62,8 kadın), kontrol grubuna ise 90 sağlıklı birey (%52,7 kadın) dahil edildi. Hasta ve kontrol grupları BBS, FRT, TUG ve SLS testleri açısından karşılaştırıldığında hasta grubundaki puanların tüm değerlendirmelerde istatistiksel olarak daha kötü olduğu görüldü. Düşme riski taşıyan AAA hastaları ileri yaşta ve hastalık süresi daha uzundu (sırasıyla $p<0,001$ ve $p<0,001$). Düşme riski olan hastalarda atak sırasındaki görsel analog ölçeği skorları, artralji varlığı ve amiloidoz varlığı daha yüksekti (sırasıyla $p=0,032$, $p=0,002$, $p<0,001$).

Sonuç: Sonuç olarak AAA hastalarında dinamik ve statik dengenin sağlıklı bireylere göre daha kötü olduğu saptandı. Hastalığın daha uzun süreli ve daha şiddetli olması, entezit ve amiloidozun varlığı dengenin bozulmasına katkıda bulunabilmektedir.

Anahtar Kelimeler: Dinamik denge, Ailevi Akdeniz ateşi, statik denge

Introduction

Familial Mediterranean fever (FMF) is distinguished by repeated attacks of arthritis, serositis, self-limiting fever and erysipelas-like erythema.[1] Musculoskeletal symptoms that include lower extremity synovitis, enthesitis, myalgia, arthralgia, and exertional leg pain are also frequently observed in patients with FMF.[2] Symptoms initiate usually before the age of 20, and the attacks last about 12 to 72 hours.[3]

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Although, patients are usually asymptomatic between attacks, in 30% of cases, subclinical inflammation persists during the attack-free period.[4] Subclinical, persistent inflammation is an insidious feature of FMF. This chronic inflammation can lead to a variety of systemic complications, including fatigue, weight loss, growth retardation, amyloidosis, anemia, and decreased bone mineral density.[5-9]

Postural balance is a complex mechanism that requires the interaction of the vestibular, visual, musculoskeletal, and somatosensorial systems. Any disruption in at least one of these systems alters the control of postural balance by causing disturbances in integration between sensory information and motor responses.[10,11] Proprioceptive feedback from joints is an important aspect to maintain balance, accordingly, in rheumatic diseases, balance may be disrupted due to swollen and tender joints. Furthermore, increased pain perception, drug side effects, decreased lower extremity muscle strength, fatigue, sleep disturbance, and decreased mobility may contribute to balance disorder. The association between balance and rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic sclerosis (SSc), and psoriatic arthritis (PsA) has been studied before.[12-15] In the literature, there are studies examining balance disorders in pediatric FMF patients and children with other rheumatic diseases.[16,17] However, balance changes in adult FMF patients have not been investigated yet. It is possible that patients with FMF will experience balance changes due to the disease progression with fatigue, comorbidities, osteopenia, synovitis, enthesitis, arthritis attacks, reduced proprioception in the lower extremities, muscle weakness and older age. The purpose of the study is to evaluate the dynamic and static balance in FMF patients.

Materials and Methods

Study Design and Participants

This study was a prospective case-control study. Patients with FMF who applied to hospital rheumatology clinic between September 2021 and September 2022 and met the modified Tel Hashomer criteria[18] were included in the study. Healthy controls were consecutively selected among volunteers without chronic diseases with similar age, gender, weight, and body mass index properties compared to patient group. Participants over the age of 18 were included in the study. Patients with neurological deficits that could lead to balance problems, lower extremity motor paresis, a history of surgical intervention in the lower extremities or vertebral problems, lower extremity arthritis or contracture, acute trauma or psychiatric disorders affecting communication, visual and vestibular disorders that could lead to balance problems, and pregnancy were all excluded from the study. Informed consent form was obtained from all participants in the study. The study was conducted in accordance with the Declaration of Helsinki and with the approval of the Ankara City Hospital Ethics Committee (IRB no: E1-21-1959, date: 25.08.2021).

Data Collection

The demographic data and comorbidities (hypertension, hypothyroidism, coronary artery diseases, chronic kidney disease, chronic obstructive pulmonary disease/asthma, diabetes mellitus) of all participants and age at diagnosis, attack characteristics (fever, pleuritic pain, erysipelas-like erythema, abdominal pain), visual analog scale (VAS) during attacks, annual number of attacks, presence of amyloidosis, *MEFV* gene mutations and medical treatments of patients with FMF were recorded. In the evaluation of the musculoskeletal system, the patients' history of arthritis, sacroiliitis, and enthesitis in the heel were investigated. The presence of sacroiliitis and enthesitis in the heel was evaluated radiographically by 2 rheumatologists with at least 5 years of radiological evaluation experience. The presence of enthesitis was determined by standard palpation methods. Enthesitis was defined as tenderness at the site of the enthesis applied with a pressure of ~4 kg/cm^2 (enough to whiten the tip of the inspector's nail) by the standard palpation approach.[19] It was noted as present or absent according to their responses to standard palpation over the entheseal regions. Enthesitis sites were evaluated over 13 sites defined with reference to the Maastricht Ankylosing Spondylitis Enthesitis score (MASES). The patients were scored between 0 and 13 points, according to MASES.[20] Disease severity was evaluated using the International Severity Scoring System (ISSF) developed by Demirkaya et al.[21] The ISSF total score ranged from 0 to 10, with a total score of ≥6 for severe disease, 3-5 for moderate disease, and ≤2 for mild disease.

Data Collection Tools

Balance Tests

The functional and dynamic balance performance of the patient group consisting of FMF patients and the control group consisting of healthy volunteers was determined by the Berg Balance scale (BBS), timed up and go (TUG) test and Functional Reach test (FRT), and their static balance was determined by right and left single leg stance (SLS) (eyes open and closed) tests.

The BBS consists of 14 parameters that assess the patient's ability to maintain balance while performing movements statically or dynamically. Each item is scored from 0 to 4,

and the maximum score of the test is 56.[22] A score of <40 is associated with an almost 100% risk of falling.[23]

The TUG test is a method used to evaluate dynamic balance and functionality. The patients were asked to get up from the chair, to return after walking 3 meters without touching anything, to walk back to the chair and return to the sitting position, and the time spent during this activity was recorded as TUG. Average time score recorded after 3 trials. Shumway Cook et al.[23] reported that individuals who completed the TUG test for 13.5 seconds or longer had a risk of falling.[24]

In the FRT test, each subject is asked to stand upright with their feet shoulder-width apart, position the arm closer to the wall at 90 degrees of shoulder flexion, and reach forward as far as possible without taking a step. The distance between the starting position of the third fingertip and the position it extends was measured and recorded in centimeters (cm). This test was repeated 3 times and average values were obtained.[25] In frail elderly patients, a reach of <18.5 cm indicates the risk of falling.[26]

For the SLS test, the patients were asked to lift one foot so that it did not touch the supporting leg. They were told to hold it in this way, and the test was terminated when the foot touched the ground again. The time elapsed during this activity was recorded as the SLS score in seconds. The test was performed in two positions for the right and left legs and with eyes open and closed. Each test was performed in triplicate, and the mean value was considered for statistical analysis in the study.[27] SLS values of <5 seconds are associated with an increased risk of falling.[28]

The FMF patients were separated into two groups based on the cut-off values in the balance tests: Those with and without the risk of falling in any of the tests.

Statistical Analysis

SPSS 22 (IBM Corp. Armonk, NY) was used for statistical analysis. Normality of continuous variables were tested with Shapiro-Wilk's test, and with plots and histograms additionally. Normally distributed variables were presented as mean ± standard deviation, and as median (interquartile range) otherwise. Categorical variables were presented as number and percentages. Continuous variables were compared between groups by Mann-Whitney U or Student t-tests according to normality. X^2 test was used to compare categorical variables. P values <0.05 were considered statistically significant.

Results

The patient group consisted of 94 FMF patients (59 females and 35 males), and the control group consisted of 90 healthy individuals (51 females and 39 males). Demographic and anthropometric characteristics were similar between groups (Table 1). Disease characteristics, genetic mutations, medical treatments, MASES and ISSFS scores of the FMF patients were shown in Table 1.

Table 1. Demographic and anthropometric features of the patient and the control groups

	Patients (n=94)	Controls (n=90)	p
Age, years, mean ± SD	37.61±10.96	37.08±10.32	0.459
Sex, female, n (%)	59 (62.8)	51 (56.7)	0.399
BMI, mean ± SD	25.02±3.94	22.96±2.99	0.083
Active smokers, n (%)	25 (26.6)	20 (22.2)	0.490
Comorbidities, n (%)			
Hypertension	15 (16)		
Chronic kidney disease	17 (18.1)		
Coronary artery disease	5 (5.3)		
COPD/asthma	2 (2.1)		
Hypothyroidism	8 (8.5)		
Age of diagnosis, years, mean ± SD	27.3±12.31		
Disease duration, years, median (IQR)	9 (11)		
Attacks per year, median (IQR)	3 (6.5)		
FMF attack characteristics, n (%)			
Fever	70 (74.5)		
Abdominal pain	91 (96.8)		
Pleuritic pain	22 (23.4)		
Arthralgia	61 (64.9)		
Erysipelas-like erythema	5 (5.3)		
VAS-pain, median (IQR)	8 (1)		
Sacroiliitis, n (%)	10 (10.6)		
Arthritis, n (%)	25 (26.6)		
Heel enthesitis, n (%)	19 (20.2)		
Amyloidosis, n (%)	17 (18.1)		
MEFV mutations, n (%)*			
M694V heterozygous	25 (26.6)		
M694V homozygous	15 (16)		
M694V/M680I heterozygous	7 (7.4)		
M694V/V726A heterozygous	8 (8.5)		
M694V/E148Q heterozygous	6 (6.4)		
E148Q heterozygous	6 (6.4)		
M680I homozygous	2 (2.1)		
V726A heterozygous	7 (7.4)		
No mutation	2 (2.1)		
Treatment agents, n (%)			
Colchicine	92 (97.9)		
Anakinra	24 (25.5)		
Canakinumab	15 (16)		
TNF-α inhibitors	6 (6.4)		
ISSF, median (IQR)	3 (3)		
MASES, median (IQR)	0.5 (3)		

**: MEFV mutation of 78 patients is known, BMI: Body mass index, , SD: Standard deviation, IQR: Interquartile range,ç COPD: Chronic obstructive pulmonary disease, FMF: Familial Mediterranean fever, ISSF: International Severity Scoring System, MASES: Maastricht Ankylosing Spondylitis Enthesitis score, TNFα: Tumor necrosis factor alpha, VAS: Visual analog scale*

Balance Test Outcomes

Static and dynamic balance test results in the groups were shown in Table 2. In all evaluations, the difference between the patient and control groups' scores on the BBS, TUG, FRT and SLS (right and left, eyes open and closed for each side) tests was statistically significant. The patient group's scores were lower. Number of patients with a score indicating risk fall according to cut-off values in any of the tests were higher in FMF group (28.7% vs. 5.5%, p<0.001).

The FMF patients were divided into two groups based on the cut-off values from the balance tests: Those who had a risk of falling in any test and those who did not. Demographic, clinical and balance parameters of the patients are shown in Table 3. FMF patients with a higher risk of falling had longer disease duration and were older (p<0.001 and p<0.001, respectively). Comorbidities such as hypertension, chronic kidney disease, coronary artery disease, and hypothyroidism were more common in patients at risk of falling (p<0.001, p<0.001, p=0.009, p=0.027, respectively). Patients who were at risk of falling had higher VAS scores during the attack, as well as higher levels of arthralgia and amyloidosis. (p=0.032, p=0.002, p<0.001, respectively). Patients at risk of falling had considerably higher ISSF and MASES scores than those who were not. (p>0.001 and p=0.001, respectively). Anakinra and canakinumab were more commonly used to treat patients at risk of falling.

Table 2. Comparison of dynamic and static balance in patient and control groups and patients at risk of falling

	Patients (n=94)	Controls (n=90)	p
BBS, score, median (IQR)	56 (3)	56 (0)	<0.0001
FRT, cm, median (IQR)	29 (9)	31 (5)	0.002
TUG, sec, median (IQR)	7.44 (1.21)	7.3 (0.46)	0.007
SLS, sec, median (IQR)			
Eyes open, (R)	34 (19.5)	39 (8.5)	0.003
Eyes closed, (R)	11 (5.93)	12 (4.03)	0.009
Eyes open, (L)	33 (20.48)	38.5 (9.25)	0.003
Eyes closed, (L)	11.2 (6)	11.45 (4.05)	0.020
Patients with fall risk, n (%)	27 (28.7)	5 (5.6)	<0.0001

BBS: Berg balance scale, cm: Centimeter, FRT: Functional reach test, L: Left, R: Right, sec: Second, SLS: Single leg stance test, TUG: Timed up and go test , SD: Standard deviation

Discussion

In our study, dynamic balance performances were evaluated with BBS, FRT, and TUG and static balance performances were evaluated with SLS. The scores were worse in FMF patients than those in healthy controls. Patients at higher risk of falling due to the cut-off value of any test were older and had the disease for longer periods of time, and amyloidosis was observed more frequently in these patients. The ISSF score, which measures disease severity, and the MASES score, which assesses the presence of enthesitis, were higher in patients with increased risk of falling.

Postural control or balance is a complex process requiring an intact network between the musculoskeletal, sensory, and cognitive systems.[29] A decrease in balance performance is observed in case of an alteration in any of these systems. Balance disorder in rheumatic diseases such as RA,[12] AS,[13] PsA,[14] SSc[15] had been investigated, however to the best of our knowledge, there is no study examining the static and dynamic balance in FMF, which may cause musculoskeletal manifestations and other complications such as amyloidosis,

Table 3. Comparison characteristics of FMF patients with and without fall risk

	FMF patients with fall risk (n=27)	FMF patients without fall risk (n=67)	p
Age, years, mean ± SD	44.18±10.83	34.97±9.92	<0.0001
Sex, female, n (%)	18 (66.7)	41 (61.2)	0.619
Age of diagnosis, years, mean ± SD	28.85±14.14	26.68±11.54	0.443
Disease duration, years, median (IQR)	14 (10)	7 (10)	0.000
Attacks per year, median (IQR)	3 (11)	3 (4)	0.596
FMF attack characteristics, n (%)			
Fever	21 (77.8)	49 (73.1)	0.640
Abdominal pain	27 (100)	64 (95.5)	0.264
Pleuritic pain	8 (29.6)	14 (20.9)	0.365
Arthralgia	24 (88.9)	37 (55.2)	0.002
Erysipelas-like erythema	2 (7.4)	3 (4.5)	0.567
Comorbidities, n (%)			
Hypertension	12 (44.4)	3 (4.5)	<0.001
Chronic kidney disease	14 (51.9)	3 (4.5)	<0.001
Coronary artery disease	4 (14.8)	1 (1.5)	0.009
Hypothyroidism	3 (4.5)	5 (18.5)	0.027
COPD/Asthma	1 (1.5)	1 (3.7)	0.501

Table 3. Continued

	FMF patients with fall risk (n=27)	FMF patients without fall risk (n=67)	p
VAS-pain, median (IQR)	8 (2)	7 (2)	0.032
Sacroiliitis, n (%)	4 (14.8)	6 (9)	0.404
Heel enthesitis, n (%)	8 (29.6)	11 (16.4)	0.149
Arthritis, n (%)	8 (29.6)	17 (25.4)	0.673
Amyloidosis, n (%)	14 (51.9)	3 (4.5)	<0.001
MEFV mutations, n (%)*			
M694V heterozygous	5 (18.5)	20 (29.9)	
M694V homozygous	10 (37)	5 (7.5)	
M694V/M680I heterozygous	1 (3.7)	6 (9)	
M694V/V726A heterozygous	1 (3.7)	7 (10.4)	
M694V/E148Q heterozygous	2 (7.4)	4 (6)	0.081
E148Q heterozygous	1 (3.7)	5 (7.5)	
M680I homozygous	0 (0)	2 (3)	
V726A heterozygous	2 (7.4)	5 (7.5)	
No mutation	0 (0)	2 (3)	
Treatment agents, n (%)			
Colchicine	26 (96.3)	66 (98.5)	0.501
Anakinra	19 (70.4)	5 (7.5)	<0.001
Canakinumab	9 (33.3)	6 (9)	0.003
TNF-α inhibitors	3 (11)	3 (4.5)	0.234
ISSF, median (IQR)	6 (3)	2 (2)	<0.001
MASES, median (IQR)	2 (5)	0 (2)	0.001

**: MEFV mutation of 78 patients is known, COPD: Chronic obstructive pulmonary disease, FMF: Familial Mediterranean fever, ISSF: International Severity Scoring System, MASES: Maastricht Ankylosing Spondylitis Enthesitis score, TNFα: Tumor necrosis factor alpha, VAS: Visual analog scale, SD: Standard deviation, IQR: Interquartile range*

all of which have potential to deteriorate balance. BBS, FRT, and TUG tests are reliable and easily applicable tests to evaluate balance in the outpatient setting.[30] In our study, when the BBS, FRT, and TUG tests were compared with age and gender-matched healthy volunteers, it was observed that the dynamic balance was worse in FMF patients. Likewise, the SLS test scores, in which static balance was evaluated in two ways (eyes open and closed), were found to be lower in FMF patients than in healthy volunteers. There may be several reasons for this postural instability observed in FMF patients. In FMF arthralgia, arthritis, and tenosynovitis, especially in the lower extremities, sacroiliitis, entheses in the lower extremities, and exertional leg pain may occur.[30] This may cause a loss of static and dynamic balance by disrupting the lower extremity proprioception of the patients. Furthermore, subclinical inflammation observed even in the attack-free period disrupts endothelial function and causes atherothrombosis, anemia, heart disease, osteoporosis, and secondary amyloidosis.[31,32] This persistent chronic inflammation associated with FMF had been shown to be an important risk factor for the development of low body mass index.[33] Studies had revealed that local or systemic inflammatory cytokines released from arthritic joints of FMF patients may play a role in bone loss and that systemic and local effects on cartilage growth in long bones may lead to osteopenia and osteoporosis.[34-36] It is a known fact that both posture disorders and balance disorders due to myopathy are seen in osteoporotic individuals.[37] In addition, the presence of slowly progressive secondary amyloid-related polyneuropathy in FMF patients with a long disease duration may also cause deterioration in balance performance.

In individuals with chronic diseases, the presence of pain, fatigue, and related sleep disorders and depression negatively affect balance performance. As with other rheumatic diseases, the presence of pain, fatigue, and sleep disorders that impair the quality of life in FMF patients had been reported in previous studies.[38,39] In a study conducted with pediatric FMF patients, it was shown that sleep quality was negatively affected as the number of attacks increased.[40] Also, Kucuksahin et al.[39] found that poor sleep quality was associated with attack frequency, fatigue, and levels of inflammatory markers during the attack. These psychological factors may be the reason for these balance disorders seen in FMF patients in our study.

The majority of the first attacks of FMF occur at the end of the teenage years.[3] Clinical episodes are accompanied by an increase in acute phase reactants such as erythrocyte sedimentation rate, C-reactive protein, serum amyloid A (SAA), and fibrinogen. All these laboratory parameters

usually return to normal levels during attack-free periods. However, it has been reported that subclinical inflammation may continue in some patients during attack-free periods and may lead to the development of amyloidosis, which can be complicated by end-stage renal disease.[31,41] High and prolonged SAA levels and prolonged disease duration are risk factors for the development of amyloidosis.[42] So far, 22 different forms of localized amyloidosis have been described.[43] Amyloid deposition can affect the central nervous system as well as peripheral motor, sensory, and autonomic nerves.[44] In addition, myopathy has been reported in patients with amyloidotic kidneys with FMF.[45] Accordingly, our results demonstrated worse postural stability and an increased risk of falling in FMF patients with a longer disease duration and presence of amyloidosis. Considering that more than one-third of adults aged 65 and over fall at least once a year, increasing age, comorbidities, gait impairment, muscle weakness, and decreased balance contribute to an increased risk of falls. Therefore, it is inevitable that increasing age and long-term disease risk will affect the risk of falling in FMF patients.

Symptoms of the disease are caused by mutations in the *MEFV* gene, which encodes the pyrin protein, which has a critical role in the regulation of inflammatory pathways. Mutant pyrin causes clinical manifestations of the disease, mostly due to overproduction of IL-1b.[46,47] ISSF score is a disease severity measurement tool related to organ dysfunction, chronic sequelae, attack frequency, attack characteristics, and acute phase reactants. In our study, the ISSF scores were found to be higher in patients with increased risk of falling, suggesting that as the disease progresses, it also affects balance performance due to chronic inflammation.

Enthesis is seen in more than 2 out of 3 patients with FMF. Irregular local auto-inflammation is the main pathogenic feature in FMF. The primary target of the disease is the serous organs, but innate immune system elements in the entheseal regions can be activated by uncontrolled minor traumatic forces. Thus, unregulated auto-inflammation driven by the innate immune system induces inflammation in these regions.[48-50] In a study, more severe disease, prolonged attacks, and high acute phase reactants were found to be related with presence of enthesitis in FMF. In addition, the frequency of arthritis, exertional leg pain, and myalgia were higher in these patients.[50] In the study of Eshed et al.[48], enthesis, arthritis, myalgia, and exertional leg pain were found to be associated with each other. In our study, the MASES enthesis score was found to be higher in patients with a high risk of falling, which may be due to this association of enthesis with other musculoskeletal symptoms.

Study Limitations

There were limitations in our study. First, due to its cross-sectional study design, effects of treatment initiation on balance were not evaluated. Second, majority of our patients were under treatment, therefore, to the best of our knowledge regarding treatment naïve patients could not be obtained. In addition, electrophysiologic evaluations were not studied as a part of the study protocol. Lastly, the relationship between the psychological and socioeconomic status and balance disorder, a factor which may play a role in balance patient perception-wise, was not assessed.

Conclusion

In conclusion, to the best of our knowledge, this study is the first to examine balance in FMF patients. Our findings showed that FMF patients had worse dynamic, functional, and static balance than healthy controls. Increased disease severity and duration, as well as the existence of enthesitis, amyloidosis, and other comorbidities, may all lead to a worsened balance. Studies with higher power would better elucidate and confirm the relationship between FMF and balance.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki and with the approval of the Ankara City Hospital Ethics Committee (IRB no: E1-21-1959, date: 25.08.2021).

Informed Consent: Informed consent form was obtained from all participants in the study.

Authorship Contributions

Concept: O.K., Design: Ş.E., Data Collection or Processing: E.A., Analysis or Interpretation: S.C.G., Literature Search: K.O., Writing: H.E.K.

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