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# The Effect of Mediterranean Diet Compliance on Cognitive Functions in COPD Patients

## Akdeniz Diyeti Uyumunun KOAH Hastalarında Bilişsel Fonksiyonlar Üzerine Etkisi

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### Öz

**Amaç:** Kronik obstrüktif akciğer hastalığı, dünya çapında önde gelen morbidite ve mortalite nedenlerinden biridir. Hastalığın ilerlemesiyle birlikte sık görülen komorbid durumlardan biri de kognitif disfonksiyondur. Bilişsel işlev bozukluğunun gelişmesi ile hastalığın tedavi yönetimi zorlaştığından, süreç sağlık çalışanları ve hastalar için zorlaşmaktadır. Akdeniz diyeti antioksidan beslenme tipine uygun bir diyettir. Diyetin KOAH üzerindeki etkilerinin bilinmesi, sağlık profesyonellerine hastalara akciğer sağlığını iyileştirme yönünde daha iyi danışmanlık yapmaları için kanıta dayalı bir yaşam tarzı yaklaşımı sağlayabilir.

**Hastalar ve Yöntem:** Çalışmamıza 49 KOAH hastası dahil edilmiştir. Bilişsel performans Montreal Bilişsel Değerlendirme ile depresyon ise Beck Depresyon Envanteri ile bir nörolog tarafından değerlendirilmiştir. Tüm hastalar Türkçeye uyarlanmış Akdeniz Diyetine Uyum Ölçeği ile değerlendirilmiştir.

**Bulgular:** Çalışmaya 49 hasta dahil edilmiştir. Çalışmamızda bilişsel işlev bozukluğu sıklığı %73.4, depresyon sıklığı %35 olarak bulunmuştur. Akdeniz Diyetine Uyum Ölçeği ile Montreal Bilişsel Değerlendirme testi sonuçları arasındaki korelasyonu analizinde Akdeniz Diyetine Uyum Ölçeğine uyumu yüksek olan hastaların Montreal Bilişsel Değerlendirme testi skorlarının da anlamlı derecede yüksek olduğu görülmüştür.

**Sonuç:** Akdeniz Diyetine yüksek düzeyde uyum gösteren KOAH hastalarında bilişsel işlev bozukluğu gelişme riski daha düşüktür.

**Anahtar Kelimeler:** KOAH, akdeniz diyeti, bilişsel fonksiyon

### Abstract

**Aim:** Chronic obstructive pulmonary disease is one of the leading causes of morbidity and mortality worldwide. Cognitive dysfunction is one of the most common comorbid conditions with disease progression. As the development of cognitive dysfunction complicates the treatment management of the disease, the process becomes more difficult for healthcare professionals and patients. The Mediterranean diet is a diet suitable for antioxidant nutrition. Knowledge of the effects of diet on COPD may provide health professionals with an evidence-based lifestyle approach to better counsel patients to improve lung health.

**Patients and Methods:** 49 COPD patients included to our study. Cognitive performance was assessed using Montreal Cognitive Assessment and depression was assessed Beck Depression Inventory by a neurologist. All patients were assessed with Turkish-adapted Mediterranean Diet Adherence Scale.

**Results:** The study included 49 patients. In our study, the prevalence of cognitive dysfunction was 73.4% and the prevalence of depression was 35%. In the analysis of the correlation between the results of the Mediterranean Diet Adherence Scale and the Montreal Cognitive Assessment test, it was observed that patients with high adherence to the Mediterranean Diet Adherence Scale also had significantly higher Montreal Cognitive Assessment test scores.

**Conclusion:** The risk of developing cognitive dysfunction is lower in patients with COPD who have high adherence to the Mediterranean Diet Adherence.

**Keywords:** COPD, mediterranean diet, cognitive function

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## INTRODUCTION

According to the latest GOLD 2023 guidelines, chronic obstructive pulmonary disease is a mortality-causing disease. The most common symptoms of the disease are dyspnea, chronic cough and accompanying sputum. The disease is diagnosed with a post-bronchodilator FEV1/FVC ratio  $< 70$  in patients with these complaints (1).

The most important known risk for developing COPD is smoking. However, smoking is not the only known risk factor. Indoor and outdoor air pollution, occupational exposure, previous infections, passive exposure to cigarette smoke are other risk factors that may lead to the development of COPD. COPD may also develop in some genetic pathologies such as alpha1-antitrypsin deficiency (2). In case of complaints in patients, COPD is diagnosed if FEV1 /FVC  $< 0.7$  in spirometry measurement after bronchodilation test. Patients with COPD most commonly complain of shortness of breath and cough with or without sputum. The disease is characterised by exacerbations. Since chronic inflammation and hypoxia are also common in patients with COPD, other comorbid conditions are often present. In the treatment management of the disease, comorbid conditions should be treated together. Because incomplete treatment of comorbid conditions may lead to exacerbation to worsen (3).

The development of oxidative stress can directly lead to lung injury, but it can also initiate an inflammatory response through the degradation of lung tissue. NF- $\kappa$ B, which plays the most important role in the inflammatory response, is involved in the initiation of lung infiltration by proinflammatory cytokines and chemotactic factors. Fibrosis developing at the end of inflammation leads to progressive deterioration in lung function. Increased oxidative, endogenous antioxidant defence in COPD also leads to a decrease in endogenous antioxidant defence (4).

While oxidative stress directly affects lung damage in COPD patients, it also leads to the progression of comorbidities with its systemic effect. Studies have been conducted to reduce oxidative stress in animal experiments in COPD, but the number of clinical studies is very few. Although antioxidant drugs are the most clinically tested drugs, there are studies showing that they can be more effective than bronchodilators and ICS. It has been shown that it can prevent exacerbations of patients, but its effect on quality of life and symptoms is unclear (5).

Diet is considered as a modifiable risk factor for disease control in chronic diseases. Recent studies

also support that it may influence many chronic diseases, including COPD (6-8). When we compared healthy controls and COPD patients, it was observed that COPD patients had diets with less fruit and vegetable intake than healthy controls. It is thought that this, together with less antioxidant content, leads to deterioration in lung function and COPD progression (9-10).

Many studies have focused on the effect of nutrients on respiration. However, the effect on respiratory health may not be fully determined, as the effect of nutrients may change with the intake of individual or combined nutrients. However, when looking at the diets of populations in general, changes in diet in the last few decades in developing countries have contributed to the increase in the prevalence of chronic diseases, including COPD (11).

The Mediterranean Diet (MedDiet) was first presented in the 1950s as the Seven Country Study. In the study, the Southern European population, which is located in the country where the olive tree grows naturally, was examined. It was observed that diseases with a high risk of death such as coronary heart disease (CHD) and cancer were significantly less common in this region compared to other countries in the world (12).

The type of diet today called the MedDiet is actually a plant-based diet. Olive oil is the main ingredient as an oil for cooking or using raw. Apart from this, adding plenty of seasonal vegetables to the diet, regular consumption of nuts and seeds, consumption of legumes several times a week, daily whole grains, consumption of fish portions two to three times a week, limited quantities of milk (yogurt, milk, cheese), flavor recipes It is recommended to consume spices and herbs, sweets several times a week, small amounts of red and processed meat, three to four eggs a week, wine in moderation (13). Prevention and treatment management of COPD is an important health problem with important social and economic problems. Comorbidities such as heart disease, osteoporosis, type 2 diabetes mellitus, lung cancer and cognitive impairment are most common in patients with COPD (14).

Cognitive assessment involves different processes that can be divided into six main neuropsychological domains: learning and memory, visuospatial and motor function, attention/concentration, language, social cognition/emotions and executive functions (15). Cognitive impairment can present with many clinical manifestations in a variety of patients. Hypoxemia

affects oxygen-dependent enzymes in COPD patients. Thus, the ground for the development of cognitive impairment is formed (16). In COPD patients, it is associated with treatment non-adherence and increased attacks, leading to increased mortality. In addition to patients' compliance with treatment, it also negatively affects their social life and has a negative impact on quality of life (17).

## PATIENTS AND METHODS

Forty-nine patients were recruited to our study in our clinic. Patients diagnosed with COPD and followed up from June 2023 to August 2023 in the Chest Diseases Clinic. Routine examinations of all patients were performed. COPD diagnosis was made according to the symptoms, physical examination, laboratory findings and pulmonary function test parameters according to the GOLD guideline. Oxygen saturation was evaluated with pulse oximetry. Patients with a score of 92% and above were included in the study. Approval was obtained from the Local Ethics Committee (Number: 2023/014). To all participants information about the study was given and written consent was obtained.

Cerebrovascular disease, diabetes, uremia and other metabolic-endocrine disorders, patients with a diagnosis and other psychiatric diseases, head trauma, interstitial lung disease, alcohol users, taking antioxidant agents, and using drugs that may affect cognitive performance were not included in the study.

In our study, the Mediterranean Dietary Adherence Scale (MEDAS) questionnaire adapted to Turkish was administered to COPD patients. MEDAS is a questionnaire consisting of 14 questions in total. Patients can score 0 or 1 point from each question. Accordingly, the highest score that can be obtained in total is 14. Patients with a score of seven or eight on the questionnaire are considered to have acceptable MEDAS adherence, while a score of nine or more is considered to have high adherence to MEDAS (18, 19). The Montreal Cognitive Assessment (MoCA) test is used to detect Mild Cognitive Impairment (MCI) and Alzheimer's disease. It consists of 11 subgroup

assessments in total. These subgroups assess attention, memory, visual structural skills, executive functions, language, and orientation. The test is scored between 0 and 30. Although the highest score is 30, scores below 21 indicate cognitive impairment (20). In order to measure the rate of depression in the patients we included in the study, we asked the patients to do the Beck Depression Inventory (BDI) (21). All cognitive and depression tests were administered to all patients by a neurologist to evaluate cognitive functions.

### Statistical Analysis

Data were analyzed using IBM SPSS Data Collection Version 6.0 and IBM SPSS Statistics Version 19. Quantitative variables are presented as mean standard deviation.  $p < 0.05$  was considered statistically significant. Descriptive statistics are reported as mean  $\pm$  SD for continuous variables and n (percent frequency) for discrete variables. Differences between groups for continuous variables were assessed by Mann-Whitney test when appropriate.

## RESULTS

Forty-nine patients were included in the study. Table 1 shows mean values of our dataset.

In the results of our study, the mean age of our patients was calculated as  $74.04 \pm 8.4$ . 26 % of our patients were female. Of the patients included in the study, 3 were under 65 years of age and 46 were over 65 years of age. According to our country's validity questionnaire, cognitive dysfunction is considered in patients with a MoCA test score of 21 and below (22). In our study, 73.4% of our patients had cognitive dysfunction according to this score. 16 of the patients were female and 33 were male. There was no significant relationship between gender and cognitive dysfunction. We administered the Beck Depression Inventory to evaluate depression in our patients. The mean questionnaire score was  $9.51 \pm 6.52$ .

In our study, the frequency of depression was found to be 35%. We found the average score to be  $6.9 \pm 2.13$ . MEDAS score was found to be greater than 7 in %48.9 of our patients.

**Table 1.** Descriptive Statistics

	Mean	Std. Deviation	N
AGE	74,04	8,443	49
BDI	9,51	6,529	49
MEDAS	6,90	2,134	49
MoCA	11,55	6,624	49

BDI; Beck Depression Inventory, MEDAS; Mediterranean Diet Adherence Scale, MoCA; Montreal Cognitive Assessment

**Table 2.** Correlation for MEDAS

		<b>N</b>	<b>Mean</b>	<b>Sum</b>	<b>P value</b>
MoCA	MEDAS <7	26	17,34	433,50	<0,05
	MEDAS >7	24	27,08	791,50	
BDI	MEDAS <7	25	27,38	684,50	<0,05
	MEDAS >7	24	22,52	540,50	
AGE	MEDAS <7	25	27,14	678,50	>0,05
	MEDAS >7	24	22,77	546,50	

BDI; Beck Depression Inventory, MEDAS; Mediterranean Diet Adherence Scale, MoCA; Montreal Cognitive Assessment.

In table 2, we evaluated the relationship between MEDAS results and cognitive tests. In the results of our study, we found that as the patients' adherence to the Mediterranean diet increased, their depression scores also decreased significantly.

The results of our study also support this. When we looked at the relationship between MEDAS results and age, no significant relationship was found in both subgroups.

We analyzed the correlation between adherence to a MEDAS and MoCA test results. As a result, it was found that patients with high adherence to a MEDAS also had significantly higher MoCA test scores. When we analyzed the patients in two subgroups as those with and without mild cognitive impairment (MoCA score < 21), the association of each group with MEDAS was found to be significant ( $p < 0,01$ ).

## DISCUSSION

Chronic obstructive pulmonary disease is a respiratory disease in which patients constantly describe shortness of breath and persistent obstruction is detected in pulmonary function tests. Extrapulmonary findings are also common in COPD. Diabetes, hypertension, heart failure and osteoporosis are the most common comorbid conditions in COPD patients, but cognitive dysfunction is also a common comorbidity that complicates compliance with treatment (23).

Hypoxia refers to a condition in which there is a lack of oxygen in the tissues. Hypoxia may occur in COPD patients with impaired lung function and due to emphysema. Thus, patients may present with symptoms such as shortness of breath, fatigue, tachycardia, and bluish discoloration of the lips and skin. In COPD, hypoxemia may occur during exertion and at rest. Hypoxemia occurring at rest indicates that the disease is serious. There is no definite information about how hypoxemia leads to cognitive dysfunction. Although the common finding in most studies is that cognitive functions are affected in stable COPD patients with hypoxemia, some studies show that

hypoxemia alone may not be responsible for cognitive dysfunction (24).

Cognitive functions normally deteriorate with aging, but this process develops more rapidly and severely in COPD patients (25). Early diagnosis of cognitive impairment may be effective in preventing the transition to dementia (26). In our study, we aimed to evaluate dietary habits in COPD patients to prevent cognitive dysfunction in the early period.

Cognitive dysfunction is a complex process that may include many findings such as clinical signs of depression (27). Therefore, in our study, we applied the Beck Depression Inventory to our patients to examine the relationship between diet and depression in our patients. We found that the tendency to depression was higher in patients with low MEDAS adherence.

It is known that the oxidative stress process and chronic inflammation have an effect on COPD progression. Antioxidants are molecules that protect the body against free radicals. In the treatment of COPD, bronchodilators and anti-inflammatory drugs are in the first place. Some studies have investigated the potential benefits of antioxidants in the treatment of COPD. It has been determined that antioxidant nutrition will prevent the progression of COPD with its anti-inflammatory effect, and thus many comorbid conditions such as cognitive dysfunction can be prevented in patients (28).

Based on the hypothesis that antioxidation would prevent the progression of COPD, we investigated the effect of this type of diet on the development of cognitive dysfunction in patients. Mediterranean-type diet is one of the most commonly practiced diets with high antioxidant content. Looking at the MEDAS compliance in our country, it was found that the average score was  $6.83 \pm 3.34$  (29). In our study, the mean value was  $6.90 \pm 2.13$ . As a result of the tests, we applied to the patients, we found that the relationship between the Mediterranean-type diet and the MoCA test measuring cognitive dysfunction and the BDI assessing depressive status was significant.

In COPD patients, exacerbations progress the

disease. With the development of chronic inflammation and hypoxia in patients, the management of comorbid conditions may also become difficult. The management of the disease enters a vicious circle, as the management of the treatment will become difficult in patients with the deterioration of cognitive functions. Therefore, stable management of the disease is effective in preventing the progression of comorbid conditions. In our study, we thought that in addition to the regular use of medical treatment, antioxidant nutrition may have a positive effect on the process. Patients can prevent the progression of COPD and common comorbidities such as cognitive dysfunction by eating an antioxidant diet together with the Mediterranean type diet, which is the closest to the diet type in our country.

When we reviewed the literature, there were studies investigating the effect of Mediterranean type diet on cognitive functions. In the studies, cognitive functions were found to be more successful in Mediterranean type nutritionists. However, we could not find any similar studies in the literature examining the effect of nutrition on cognitive functions in COPD patients. Therefore, we think that it will be guiding for future studies. As in many studies, there are deficiencies in our study. The missing aspect of our study is the small number of patients.

## CONCLUSION

As a result, we determined that the Mediterranean type diet, which is an antioxidant diet, is effective on cognitive dysfunction in COPD patients. Antioxidant nutrition may prevent the progression of many pathologies in COPD patients in the long term, but although antioxidants show promise, they cannot be recommended as a substitute for standard COPD treatments prescribed by healthcare professionals. Further studies are needed to investigate this relationship in COPD patients.

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# Patient Management and Surgical Results in Osteochondroma Cases

## Osteokondrom Vakalarında Hasta Yönetimi ve Cerrahi Sonuçlarımız

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### Öz

**Amaç:** Bu çalışmanın amacı üçüncü basamak bir onkoloji merkezinde cerrahi tedavi uygulanmış osteokondrom tanılı 121 hastanın demografik verilerini, tümörlerin tanı ve tedavi yöntemini ve cerrahi sonrası klinik sonuçlarını sunmaktır.

**Hastalar ve Yöntem:** 2009-2019 tarihleri arasında osteokondrom tanısı alan ve cerrahi tedavi uygulanan 18-65 yaş arasında olan ve en az 1 yıl takip süresi olan 121 hasta retrospektif olarak incelenerek dahil edildi. Tümör boyutu ve kıkırdak kep kalınlığının herediter tümörü soliter tümörden ayırt etmek için anlamlı cutoff değerlere sahip olup olmadığı ROC analizi ile incelendi.

**Bulgular:** Hastaların yaş ortalaması 31.7±12,9 yıldır ve %57'si erkektir. Hastaların tümör boyutu ortalaması 43,4 mm ve kıkırdak kep kalınlığı ortalaması 7,1 mm olarak hesaplanmıştır. Ayrıca, çalışmada incelenen hastaların %16,5'inde herediter osteokondrom tanısı, %1,7'sinde ise malign transformasyon sonucu kondrosarkom tespit edilmiştir. Herediter osteokondrom tanısı almış hastaların tümör boyutu ve kıkırdak kep kalınlığı soliter hastalardan anlamlı olarak yüksek bulunmuştur. Tümör boyutu ve kıkırdak kep kalınlığı, herediter tümörleri soliter tümörlerden ayırt etmede kullanılabilecek önemli göstergeler olarak tespit edilmiştir. ROC analizi sonucu kıkırdak kep kalınlığı için kesme değeri 7,5 mm, tümör boyutu için kesme değeri 49 mm olarak belirlenmiştir.

**Sonuç:** Osteokondrom tedavisi genellikle cerrahi müdahale ile başarılı bir şekilde tedavi edilebilir ve cerrahi sonrası komplikasyonlar nadirdir. Bu çalışma, osteokondrom hastalarının tedavi ve takibinde klinik kararları desteklemek için önemli bilgiler sağlamaktadır.

**Anahtar Kelimeler:** Osteokondrom, ekzositoz, total eksizyon, kıkırdak kep

### Abstract

**Aim:** The aim of this study is to present the demographic data, diagnostic and treatment methods of tumors, and postoperative clinical outcomes of 121 patients diagnosed with osteochondroma who underwent surgical treatment at a tertiary oncology center.

**Patients and Methods:** A total of 121 patients between 18 and 65 years of age, diagnosed with osteochondroma and treated surgically, with a minimum follow-up period of 1 year, were retrospectively included in the study between 2009 and 2019. The tumor size and cartilage cap thickness were analyzed with ROC analysis to determine significant cutoff values for distinguishing hereditary tumors from solitary tumors.

**Results:** The average age of the patients was 31.7±12.9 years, and 57% of the patients were male. The mean tumor size was calculated as 43.4 mm, and the mean cartilage cap thickness was 7.1 mm. In addition, hereditary osteochondroma was diagnosed in 16.5% of the patients, and chondrosarcoma resulting from malignant transformation was detected in 1.7% of the cases. The tumor size and cartilage cap thickness in patients with hereditary osteochondroma were significantly higher than in solitary cases. The tumor size and cartilage cap thickness were identified as important indicators for distinguishing hereditary tumors from solitary tumors. ROC analysis resulted in a cutoff value of 7.5 mm for cartilage cap thickness and 49 mm for tumor size.

**Conclusion:** Osteochondroma treatment can generally be successfully managed with surgical intervention, and postoperative complications are rare. This study provides important information to support clinical decisions in the treatment and follow-up of osteochondroma patients.

**Keywords:** Osteochondroma, exostosis, total excision, cartilage cap

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## INTRODUCTION

Osteochondromas are the most common benign bone tumors. They account for 3% of the general population and make up 20-50% of all benign bone tumors and 10-15% of all bone tumors. Patients usually present with a long-standing, slow-growing, hard, painless, and palpable swelling. (1,2). Osteochondromas are cartilage-capped bony protrusions or exostoses growing outward from the bone surface. The cartilage cap is covered by a fibrous perichondrium with continuity to the underlying bone periosteum (3). They can occur in any bone developing through endochondral ossification. They most commonly occur in the metaphyseal regions of long bones and can rarely occur at the metaphyseal-diaphyseal junction. They commonly affect the areas around the knee and the long bones of the arm and forearm (4). Osteochondromas can have various shapes, such as round pedunculated, mushroom-like, cauliflower-like, horn-like, or sessile. Most osteochondromas are solitary lesions, with Hereditary Multiple Exostosis (HME) accounting for about 15% of osteochondromas (2, 5). Recent studies have indicated that the pathogenesis of hereditary multiple osteochondromas is characterized by genetic mutations. Germ cell mutations in the exostosin 1 (EXT1) and exostosin 2 (EXT2) genes on chromosomes 8 and 11 are associated with the disease (6-8). The cartilage cap in osteochondromas is generally about 2-3 mm thick. In actively growing benign osteochondromas in adolescents, the cap may be 1-3 cm thick. Particularly in adults, a cartilage cap thickness exceeding 2 cm and irregularities in the cap favor secondary chondrosarcoma (9). The most significant findings supporting malignant transformation include sudden rapid growth of the lesion, continued growth of the lesion despite completion of maturation, and pain in the absence of fractures, bursitis, or nerve compression.

In the follow-up radiographs, an increase in the size of the lesion and the presence of pain, along with the presence of amorphous calcification on the graph, erosion of the cartilage septa (10), the development of cartilage cap with a thickness of more than 2 cm on MRI and 1 cm on CT (11, 12), and scattered calcification in the cartilage cap on CT (11, 13) are findings in favor of malignant transformation.

The indicators of the success of surgery and patient characteristics are highly debatable. This is because most studies related to Hereditary Multiple Exostosis (HME) are retrospective, have incomplete information,

and have small sample sizes. The purpose of this study is to evaluate the demographic data, diagnostic and treatment methods of benign tumors diagnosed as osteochondroma in 121 patients who underwent surgical treatment.

## PATIENTS AND METHODS

This study is a cross-sectional study. A total of 121 patients diagnosed with osteochondroma who underwent surgical treatment between January 2009 and December 2019 at our tertiary oncology center were included. Inclusion criteria were patients between 18 and 65 years of age with a tumoral lesion who were histopathologically diagnosed with osteochondroma and treated surgically by our team, currently alive with at least one year of follow-up at our hospital. Exclusion criteria were as follows patients with pre-diagnosed osteochondroma who did not undergo surgical treatment, patients who discontinued follow-up, patients currently alive but with less than one year of follow-up, patients with histopathology indicating a diagnosis other than osteochondroma, and patients with unavailable follow-up information.

All research data were obtained through examination of patient system records and archive files, and through face-to-face and telephone interviews; no new blood, tissue samples, or imaging tests were requested from any patient within the scope of the research. From the patients' files, age, gender, tumor localization, histopathological diagnosis, preoperative symptoms and duration, applied surgical procedures, presence of recurrence during follow-up, date of diagnosis, date of surgical treatment, and follow-up duration were retrospectively investigated. Institutional Ethics Committee approval was obtained before starting the study (Ethics committee approval number: 2020-12/904). The average tumor size was calculated using macroscopic pathological measurement records and tumor sizes from MRI reports.

### **Statistical Analyses**

The research data were statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 22.0 for Windows. Descriptive statistics were presented as numbers, percentages, mean  $\pm$  standard deviation, and median (minimum-maximum values) for categorical and continuous variables. The normality of continuous variables was evaluated using visual and analytical methods. Since the data of continuous variables did not follow a normal distribution, the Mann-Whitney U test and chi-square test were used for comparison analysis

between groups for non-normally distributed data and categorical variables, respectively. ROC analysis was used to determine significant cutoff values for tumor size and cartilage cap thickness to distinguish hereditary tumors from solitary tumors. The cutoff point was determined using the Youden index. The level of statistical significance in this study was set at  $p \leq 0.05$ .

### RESULTS

A total of 121 patients, 69 of whom were male, with a mean age of  $31.7 \pm 12.9$  were included in this study. When the distribution of patients' presenting symptoms was examined, 71.9% had swelling, 52.9% had pain, 21.5% had limited mobility, and 17.4% had deformity. Incidental diagnosis was made in 21.5% of the patients (Table 1). The mean follow-up period of the patients participating in the study was  $51.3 \pm 29.7$  months, and 53.7% of the tumors were located on the right side. Most commonly observed localizations were distal femur (32.7%), proximal tibia (15.7%), and proximal femur (8.3%) (Figure 1). The mean tumor size of the patients was  $43.4 \pm 26.5$  mm, and the mean cartilage cap thickness was  $7.1 \pm 5.1$  mm. In terms of

hereditary traits, 20 patients (16.5%) were diagnosed with hereditary osteochondroma. Chondrosarcoma resulting from malignant transformation was detected in 1.7% of the patients. When tumor types were examined, 50.4% were pedunculated. Among the 61 patients with pedunculated tumors, the most common types were cauliflower-like (45.9%) and horn-like (32.8%). Only two patients underwent wide resection, while 98.3% underwent total excision. The radiograph and peroperative images of a patient who underwent total excision are presented in Figure 2. The most common reason for surgery was cosmetic (43.8%). Postoperative complications included peroneal nerve injury in one patient. During follow-up, recurrence was observed in three patients (2.5%), and total excision was performed in these cases (Table 2).

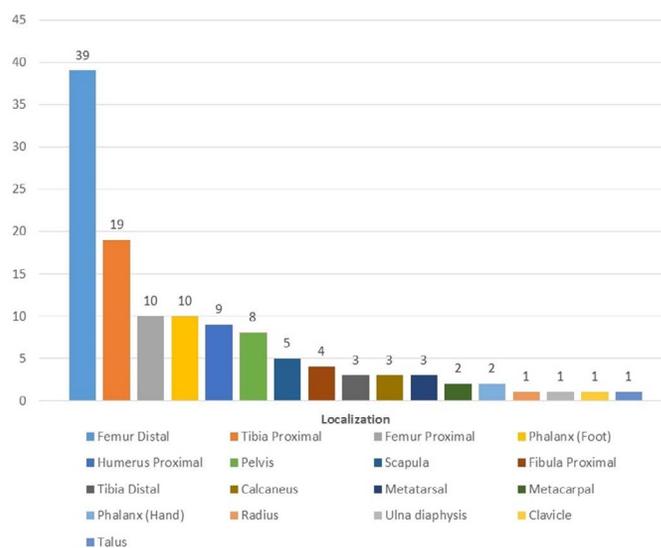
There was a statistically significant correlation between tumor size and cartilage cap thickness ( $r = 0.642$ ;  $p < 0.001$ ). There were no significant differences in tumor size and cartilage cap thickness between the pedunculated and sessile tumor groups ( $p > 0.05$ ). The distribution of malignant transformation and hereditary traits among the groups did not show statistically significant differences ( $p > 0.05$ ).

The median age of patients in the hereditary tumor group was 32, while it was 28 in the solitary group, and the ages of the groups were found to be similar ( $p = 0.586$ ). There were no significant differences in gender between the groups ( $p = 0.655$ ). There

**Table 1.** Demographical and Clinical Features of the Patients

Parameters (N=121)	
Gender, n (%)*	
Male	69 (57)
Female	52 (43)
Age, years	
Mean±sd	31.7±12.9
Median (min-max)	28 (11-70)
Swelling, n(%)	
No	34 (28.1)
Yes	87 (71.9)
Pain, n(%)	
No	57 (47.1)
Yes	64 (52.9)
Deformity, n(%)	
No	100 (82.6)
Yes	21 (17.4)
Incidental, n(%)	
No	95 (78.5)
Yes	26 (21.5)
Neurovascular Involvement, n(%)	
No	119 (98.3)
Yes	2 (1.7)
Movement Limitation, n(%)	
No	95 (78.5)
Yes	26 (21.5)

sd: standard deviation \* The percentage of the column has been used



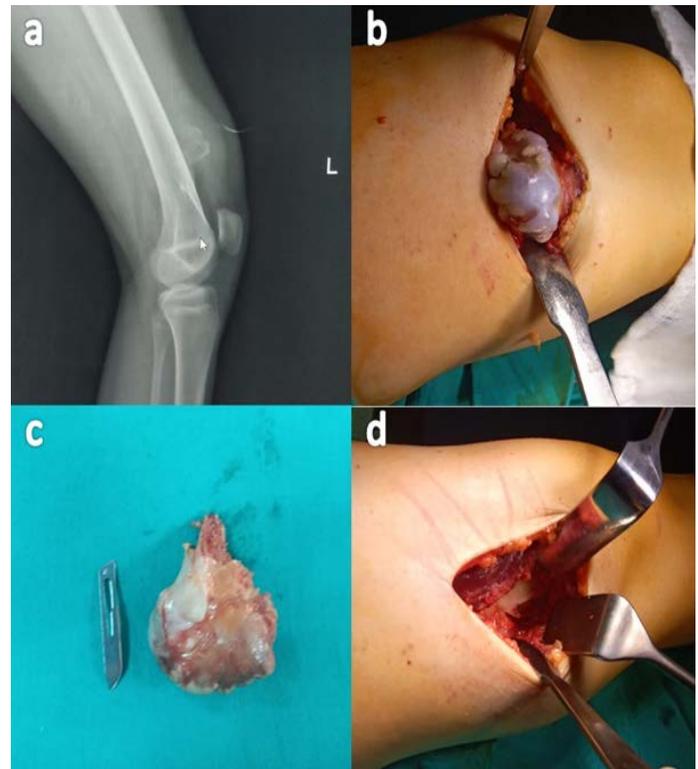
**Figure 1.** Distribution of osteochondromas by localization

**Table 2.** Diagnosis and Follow-up Features of the Patients

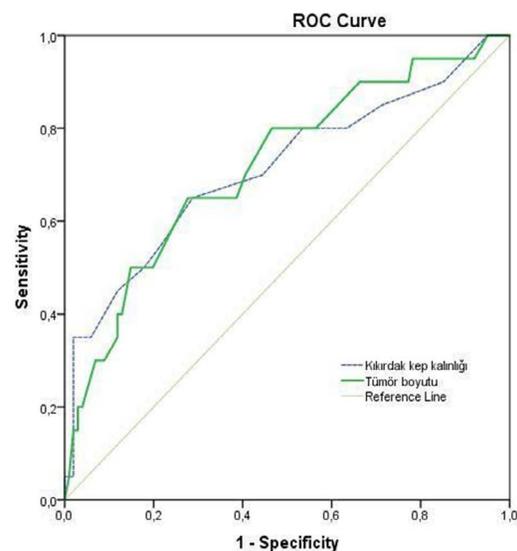
<b>Parameters (N=121)</b>	
Tumor size, mm	
Mean±sd	43.4±26.5
Median (min-max)	40 (5-130)
Cartilage cap width, mm	
Mean±sd	7.1±5.1
Median (min-max)	6 (1-33)
Familial heritance, n(%)	
Hereditary	20 (16.5)
Solitary	101 (83.5)
Malignant transformation, n(%)	
No	119 (98.3)
Yes	2 (1.7)
Histopathology, n(%)	
Osteochondroma	119 (98.3)
Chondrosarcoma	2 (1.7)
Tumor Type, n(%)	
Pedunculated	61 (50.4)
Sessile	60 (49.6)
Pedunculated tumor shape (n=61), n(%)	
Cauliflower	28 (45.9)
Horn	20 (32.8)
Mushroom	8 (13.1)
Subungual	5 (8.2)
Surgical treatment, n(%)	
Total excision	119 (98.3)
Wide resection	2 (1.7)
Surgical Indication, n(%)	
Cosmetic	53 (43.8)
Pain	34 (28.1)
Movement Limitation	21 (17.3)
Deformity	11 (9.1)
Neurovascular Involvement	2 (1.7)
Postoperative Complication, n(%)	
No	120 (99.2)
Yes (Peroneal palsy)	1 (0.8)
Recurrence, n(%)	
No	118 (97.5)
Yes*	3 (2.5)

sd: standard deviation \* 3 patients total excision

were no differences between the groups in terms of follow-up period, surgical treatment, and recurrence status ( $p > 0.05$ ). The median tumor size was 55 mm in the hereditary group and 35 mm in the solitary group. The tumor size of the hereditary group was significantly higher than that of the solitary group ( $p = 0.002$ ). The median cartilage cap thickness in the hereditary group was 9.5 mm, significantly higher than the solitary group's median value of 6 mm ( $p = 0.003$ ) (Table 3). ROC analysis was conducted to test the predictive power of tumor size and cartilage cap thickness in distinguishing the hereditary tumor group from the solitary group. Accordingly, the AUC



**Figure 2.** The radiograph (a) and peroperative images (b,c,d) of a patient who underwent total excision



**Figure 3.** ROC curves pertaining to predictive power of cartilage cap thickness and tumor size for hereditary osteochondroma

**Table 3.** Comparison of the Hereditary and Solitary Groups

	Familial Inheritance		p
	Hereditary (n=20)	Solitary (n=101)	
(N=121)			
Age, years			0.586*
Mean±sd	32.5 ±12.2	31.6±13.2	
Median (min-max)	32 (18-64)	28 (11-70)	
Gender, n (%)			0.655**
Male	10 (50)	59 (58.4)	
Female	10 (50)	42 (41.6)	
Follow-up Period, months			0.691*
Mean±sd	48.6±28.9	51.8±29.9	
Median (min-max)	42 (12-120)	48 (12-120)	
Surgical Treatment, n(%)			0.304**
Total excision	19 (95)	100 (99)	
Wide resection	1 (5)	1 (1)	
Recurrence, n(%)			0.421**
No	19 (95)	99 (98)	
Yes	1 (5)	2 (2)	
Tumor Size, mm			0.002*
Mean±sd	62.6±33.7	39.6±23,3	
Median (min-max)	55 (10-130)	35 (5-130)	
Tumor Size, n(%)			0.003**
<49 mm	7 (35)	73 (72.3)	
≥49 mm	13 (65)	28 (27.7)	
Cartilage cap width, mm			0.003*
Mean±sd	11.1±7.5	6.3±4.1	
Median (min-max)	9,5 (2-33)	6 (1-28)	
Cartilage Cap Width, n(%)			0.004**
<7,5 mm	7 (35)	72 (71.3)	
≥7,5 mm	13 (65)	29 (28,7)	
Malignant Transformation, n(%)			0.304**
No	19 (95)	100 (99)	
Yes	1 (5)	1 (1)	
Tumor Type, n(%)			0.237**
Pedunculated	13 (65)	48 (47.5)	
Sessile	7 (35)	53 (52.5)	
Pedunculated Tumor Shape (n=61), n(%)			0.453**
Cauliflower	6 (46.2)	22 (45.8)	
Horn	4 (30.8)	16 (33,4)	
Mushroom	3 (23)	5 (10.4)	
Subungual	0	5 (10.4)	

\*1Mann-Whitney U Test \*\*Chi-square Test

**Table 4.** ROC Analysis Results in Diagnostic Approach to Hereditary Tumor

	AUC (95% CI)	P	Cut-off value	Sensitivity (%)	Specificity (%)	+LHR	PPV (%)	NPV (%)	Max Youden Index
Cartilage cap	0,712 (0,572-852)	0.003	≥7.5	65	71.3	2.3	31	91.1	0.36
Tumor Size	0,720 (0,593-0,848)	0.002	≥49	65	72.3	2.3	31.7	91.3	0.37

+LHR: Positive Likelihood Ratio, PPV: Positive Predictive Value, NPV: Negative Predictive Value

was 0.720 ( $p = 0.002$ ) for tumor size and 0.712 ( $p = 0.003$ ) for cartilage cap thickness (Figure 3). Both variables were found to have the ability to distinguish hereditary tumors from solitary tumors and were statistically significant. The cutoff value for cartilage cap thickness was determined to be 7.5 mm, and for tumor size, it was 49 mm. The sensitivity, specificity, positive predictive value, and negative predictive value for the cutoff values are presented in Table 4.

## DISCUSSION

Osteochondromas, or osteochondrogenic exostoses, are the most common benign bone tumors. As they can involve almost the entire skeletal system and are the most common benign bone tumor, they require consideration of various anatomical, surgical, and clinical sensitivities. On the other hand, especially in the hereditary form, such as in the case of multiple hereditary exostoses, the risk of malignant transformation to chondrosarcoma necessitates the establishment of a sensitive clinical examination and follow-up algorithm, despite being benign tumors. This study aims to present data on surgical treatment of patients diagnosed with osteochondroma at a tertiary oncology center. Demographic data of patients, diagnostic and treatment methods of tumors, and postoperative clinical outcomes were evaluated. There are many studies in the literature on the frequency, symptoms, treatment, and outcomes of osteochondromas. The results of this study are considered to be consistent with the literature and may be useful in the management and improvement of surgical outcomes for patients with osteochondroma.

Malign transformation, the most serious complication of osteochondromas, usually occurs within the cartilaginous cap and leads to the development of secondary chondrosarcoma (14). Studies correlating cartilage cap thickness and malignant transformation are available in the literature (1, 9). Cartilage cap thickness greater than 3 cm in children and 2 cm in adults has been reported as a sign of malignancy (15, 16). Studies have indicated that malignant transformation occurs in approximately 1% of solitary osteochondromas and 10% of Hereditary Multiple Exostoses (HME) cases (17, 18). In our study, 16.5% of patients were diagnosed with hereditary osteochondroma, and 1.7% were detected to have chondrosarcoma resulting from malignant transformation. No studies were found in the literature that specifically used cartilage cap thickness and tumor size to distinguish

between solitary and hereditary osteochondromas. Previous research has shown that the hereditary form of osteochondromas carries a higher risk of malignant transformation (1, 6, 7, 17, 18). Therefore, the ability to differentiate between the solitary and hereditary forms of osteochondromas early on is crucial. The findings of our study showed that patients with a diagnosis of hereditary osteochondroma had significantly higher tumor size and cartilage cap thickness compared to solitary patients.

Spontaneous regression has been described in both solitary and multiple hereditary forms in the literature (19). There are two main hypotheses for spontaneous regression. Copeland and Castriota-Scanderbeg suggested that this may occur due to impaired blood supply following repair and remodeling activation after a fracture in the tumor (20). According to this theory, it can be assumed that pedunculated lesions may have a higher likelihood of fractures, and therefore spontaneous regression may be more common in pedunculated lesions. Another theory proposed by Parling et al. is that if the tumor stops growing before skeletal maturation is completed, it will incorporate with the growing metaphysis and undergo resolution (21). In this study, spontaneous regression was not observed in any of the patients during follow-up.

Regarding the timing of surgical treatment, there is no definitive recommendation in the literature. However, in patients with neurological symptoms, surgical decision-making is recommended to be prompt, though not urgent. Generally, there is no evidence that delayed surgery poses a problem in terms of the outcomes of symptoms. There are studies in the literature stating that weakness due to nerve compression continued in the postoperative period, and that early surgery was the correct decision (22, 23). Weinar and Hoyt suggested early surgery due to increased anteversion and coxa valga in 25 patients with osteochondromas around the minor trochanter (24).

The limitations of this study include its retrospective design and the fact that it includes data from only a single oncology center, limiting the generalizability of the results. Therefore, larger-scale and prospective studies are needed.

In conclusion, this study provides important information about the management and surgical outcomes of patients with osteochondroma. Moreover, it demonstrates the need for special attention to hereditary tumors and that tumor size and cartilage

cap thickness are important factors for the follow-up and treatment of patients. Lack of sufficient knowledge in this regard can lead to delayed diagnosis and inadequate treatment with serious consequences for the affected patient.

**Conflict of interest:** Authors declare that there is no conflict of interest between the authors of the article.

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# Konsantrik ve Eksantrik Egzersizin Dirsek Eklemi Kuvveti Üzerindeki Etkilerinin Karşılaştırılması

## A Comparison of The Effects of Concentric Versus Eccentric Exercise on Force at The Elbow Joint

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### Öz

**Amaç:** Bu çalışmanın amacı eksantrik odaklı direnç egzersizinin kas gücüne olan etkinliğini konsantrik odaklı direnç egzersizi ile karşılaştırmaktır.

**Hastalar ve Yöntem:** Çalışma kasım 2021-haziran 2022 tarihlerinde elit sporcu (grup 1, n= 10), başlangıç sporcu (grup 2, n=12) spor yapmayan (grup 3, n=12) olarak 34 katılımcı ile tamamlandı. Çalışmaya katılan bireylerin yaş, kilo, cinsiyet, dominant üst ekstremitesi (Edinburg Anketi), hipermobilité durumu (Modifiye Beighton Hipermobilité Testi), yayı tutan kolu kaydedildi. Her iki ekstremitenin m. biceps brachii ve m. triceps brachii kasları kuvveti, el kavrama gücü, pinç gücü ve reaksiyon hızı değerlendirildi. Veriler uygun istatistiksel yöntemlerle değerlendirildi.

**Bulgular:** Gruplara göre karşılaştırıldığında; grup 1 ve grup 3 arasında her iki tarafın kas gücünde ve pinç güçlerinde ve her iki taraf reaksiyon hızlarında anlamlı farklılık belirlendi (p<0,05). Grup 2 ve grup 3 arasında ise sol pinç gücü ve sol reaksiyon hızında anlamlı fark tespit edildi (p<0,05).

**Sonuç:** Her iki direnç antrenman türü de kol gücünü, pinç gücünü ve reaksiyon hızını etkili bir şekilde artırdı. Ancak eksantrik odaklı direnç egzersizin kol kaslarının performansını konsantrik egzersizlere göre daha fazla artırdığı belirlendi.

**Anahtar Kelimeler:** Ekstantrik egzersiz, hand- held dinamometresi, kas gücü, konsantrik egzersiz, okçu.

### Abstract

**Aim:** The aim of this study is to compare the effectiveness of eccentric-focused resistance exercise on muscle strength with concentric-focused resistance exercise.

**Patients and Methods:** The study was conducted with 34 participants from November 2021 to June 2022, categorized as elite athletes (group 1, n=10), novice athletes (group 2, n=12), and non-athletes (group 3, n=12). Participants' age, weight, gender, dominant upper extremity (Edinburgh Inventory), hypermobility status (Modified Beighton Joint Hypermobility Test), and the arm used for archery were recorded. Evaluation included muscle strength of both extremities' m. biceps brachii and m. triceps brachii, handgrip strength, pinch strength, and reaction time.

**Results:** When compared between groups, significant differences were found in muscle strength and pinch strengths on both sides, as well as reaction times on both sides between group 1 and group 3 (p<0.05). Significant differences were also observed in left pinch strength and left reaction time between group 2 and group 3 (p<0.05).

**Conclusion:** Both types of resistance training effectively increased arm strength, pinch strength, and reaction time. However, eccentric-focused resistance exercise was found to enhance the performance of arm muscles more than concentric exercises

**Key words:** Eccentric exercise, hand-held dynamometer, muscle strength, concentric exercise, archer.

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**Açıklama:** Yazarların hiçbirisi, bu makalede bahsedilen herhangi bir ürün, aygıt veya ilaç ile ilgili maddi çıkar ilişkisine sahip değildir. Araştırma, herhangi bir dış organizasyon tarafından desteklenmedi. Yazarlar çalışmanın birincil verilerine tam erişim izni vermek ve derginin talep ettiği takdirde verileri incelemesine izin vermeyi kabul etmektedirler.



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## GİRİŞ

Okçuluk özellikle omuz kuşağı ve önkol bölgesinin kuvvet ve enduransına dayanan bir spordur. İleri düzey bir sporcunun antrenmanlarında statik ve dinamik hareketleri içeren performansında üst ekstremité için yüksek hassasiyet ve güçlü koordinasyona sahip olması beklenir (1,2). Dışarıdan bakınca fazla bir efor gerektirmiyor gibi görünen okçuluk sporu aslında eğitim ve yarışmalarda beklentileri karşılamak için uzun süreli odaklanmaya, doğru bir postüre, esnekliğe ve kuvvete ihtiyaç duyar (3). Her ok atışında aktif kontraksiyon sağlayan kaslar şunlardır; musculus (m.) trapezius, m. deltoideus, m. rhomboideus major ve minor, m. biceps brachii ve m. triceps brachii, m. subraspinatus, m. pectoralis major ve minor, m. flexor digitorum superficialis ve m. extensor digitorum (4). Okçulukta üst ekstremité kinezyolojik hareket incelenmiştir. Buna göre; bir okçu hedefe doğru dirsek ekstansiyonda olan kol ile statik olarak yayı iterken, diğer kol ile çekme aşamasının başlangıcından serbest bırakma anına kadar dinamik olarak kırışı çeker. Yani sağ tarafı dominant olan bireylerde; sol kol yay kolu olup (m. biceps brachii eksantrik, m. triceps brachii konsantrik kasılır), sağ kol kırış kolu olup (m. biceps brachii konsantrik, m. triceps brachii eksantrik) kasılır. Atış performans başarısı için kol kaslarının agonist ve antagonist kasları arasındaki kas gücü dengesinin ve koordinasyonunun gerekliliği anlaşılmıştır (2).

Eksantrik kas kasılmasında kasılan kas zorla uzatılır. Konsantrik kas kasılmalarında ise kasın boyu kısalır. Bu kasılma farklılığının etkileri ve birbirinden üstünlükleri merak konusudur. Eksantrik egzersizler özellikle yokuş aşağı yürüyüş, kayak ve binicilikte önemli bir bileşendir. Bazı aktiviteler ise hem eksantrik hemde konsantrik kasılmaları birlikte gerektirir. Bisiklete binme, yüzme ve kürek çekme bu egzersizlere örnektir (5).

Yapılan bilimsel araştırmalarda kas kuvvetlendirme egzersiz seçimi konusunda çeşitli klinik tanı almış hastalıklarda veya spor gruplarında farklı görüşler belirtilmiştir (6-9). Sınırlı sayıda çalışmaya göre, eksantrik kasılmaların, konsantrik kasılmalardan daha düşük metabolik, kardiyak ve nöral aktiviteyle kas gücünü ve hipertrofiyi artırdığı belirtilmiştir (6,10) Kuvvet antrenmanı yapan genç erkekler arasında bile, kuvvet antrenmanı sırasında vurgulanan eksantrik yükleme, eş merkezli antrenmandan daha fazla izometrik torku ve kas aktivasyonunu artırır (6). Sağlıklı yetişkinlerde her iki dirençli eğitimin kas hipertrofisini artırdığı ancak birbirine göre kasın

mimarisinden farklılıklar oluşturduğu belirlenmiştir. Eksantrik egzersizlerin kasın fasikül uzunluğu daha fazla etkilediği ve kasın distal uçlarında hipertrofinin daha çok geliştiği; konsantrik egzersizlerden sonra ise kas hipertrofisinin büyük ölçüde kasın orta kısmında meydana geldiği ve pennasyon açısında değişikliklere neden olduğu belirtilmiştir (8)

Tüm bu belirtilenlere rağmen hangi dirençli egzersizin kas kuvvetini daha fazla artırdığı konusunda çelişkiler devam etmektedir. Bu çelişkileri ortadan kaldırabilmek için planlanan bu çalışmada bireysel farklılıkları en aza indirebilmek için okçuluk sporu tercih edilmiştir. Okçuluk sporunda aynı kişinin kırış kolunda m.biceps brachii konsantrik, antagonist kası m. triceps brachii ise eksantrik kasılırken yay kolunda ise her iki kas içinde durum tam tersidir. Dolayısıyla okçuluk sporu hem iki dirençli kasılma tipinin aynı kas gücüne olan etkisine hem de aynı kişi üzerinde antagonist kasların birbirine göre kas gücü durumlarını değerlendirme imkanı sağlar.

Bu çalışmanın amacı üst ekstremité konsantrik ve eksantrik egzersizlerin kas gücü üzerindeki etkilerinin okçularda anlaşılması ve yay kolu ile kırış kolu arasındaki reaksiyon hızı farklılıklarını araştırmaktır. Aynı bireyde bu iki tip egzersizin etkilerinin değerlendirildiği herhangi bir çalışmaya rastlanılmamıştır. Kesitsel ve tabakalı randomize olarak dizayn edilen bu çalışma aynı bireylerde her iki tip egzersizin değerlendirilmesi konusunda bir ilk olmaktadır.

## HASTALAR VE YÖNTEM

### *Araştırma Modeli*

Araştırmanın modeli okçuluk sporu ile ilgilenen bireylerde, sporcu olma süresi ile kırış ve yay kolunun dirsek fleksör ve ekstansör kaslarının kas gücü, pinç gücü ve reaksiyon zamanları arasındaki ilişkinin belirlenmesi amacı ile yapılan kesitsel bir araştırmadır.

### *Örneklem*

Araştırma, Konya Gençlik ve Spor Müdürlüğü'nün Okçuluk Spor Kulübü okçuları ile yürütülmüştür. Araştırmanın evrenini okçuluk branşında devam eden veya yeni başvuru yapan bireyler oluşturur. Araştırmanın örnekleme için G Power yazılımı kullanılmıştır. Yapılan güç analizinde Brockett ve ark.'larının (5) elde ettikleri veriler dikkate alınarak örneklem sayısı %95 güven (1- $\alpha$ ), %95 test gücü (1- $\beta$ ) ve d=0.5 etki büyüklüğü analizine göre her grup 10 birey ve %10 hata payı düşünülerek toplam katılımcı sayısı 33 olarak belirlendi.

### **Veri Toplama Araçları ve Süreçleri**

Araştırma için Necmettin Erbakan Üniversitesi, ilaç ve tıbbi cihaz dışı araştırmalar etik kurulundan 2021/3219 karar sayılı izin alınmıştır. Çalışma 2021 kasım-2022 haziran tarihleri arasında gerçekleştirilmiştir. Konya Gençlik ve Spor Müdürlüğü'nün kapsamında yürütülen okçuluk branşına hafta da en az 3 gün devam eden ve henüz yeni okçuluk sporuna başlayan 81 birey bilgisayar destekli program kullanılarak tabakalandırılmış blok randomizasyon yöntemi ile çalışmaya dahil edildi. Bu bireylerin 47 tanesi daha önce omuz v.b. cerrahi hikayelerinin olması, üst ekstremitede ağrı, hipermobilité, genel sağlık sorunlarının varlığı çalışma dışı bırakılmıştır. Çalışmaya katılmaya gönüllü olan uygun kriterlerdeki bireylerin spor geçmişleri sorgulandı. Buna göre 2 yıl ve üzerinde okçuluk sporu yapan sporcular Grup 1 (elit sporcu), 2 yıl ve altında okçuluk sporu yapanlar Grup 2 (başlangıç sporcu) ve henüz okçuluk sporuna başlamamış ancak kayıt yaptıran bireyler ise Grup 3 (kontrol grup) olarak çalışma içerisinde gruplandırıldı ve çalışma 34 katılımcı ile yürütüldü. Değerlendirmeler Şubat-Haziran 2022 tarihleri aralığında yapıldı. Katılımcıların değerlendirilmelerinin yapılmasında ve elde edilen verilerin yorumlanmasında araştırmacılar kördü.

Tüm katılımcıların onamları alınarak değerlendirmeleri yaklaşık 30 dakika süresi içerisinde yapıldı. Parametreler için sosyodemografik bilgiler, el tercihi için; Edinburg El Tercihi Anketi, eklem mobilitesinden değerlendirilmesi için Beighton mobilite değerlendirme yöntemi, kas gücü için; Hand-Held Dinamometre ve reaksiyon zamanı için; Nelsonun ölçümü kullanıldı.

### **Sosyodemografik değerlendirme:**

Çalışmaya katılan tüm sporcuların cinsiyet, yaş, boy, kilo, eğitim durumu, yayı tutan kol tercihleri, antreman yapma süreleri (yıl), antreman yapma süreleri (gün/hafta), antreman yapma süreleri (saat/gün) araştırmacı tarafından teke tek görüşme yoluyla kayıt altına alındı. Edinburg El Tercihi Anketi kullanılarak el tercihi sorgulandı. Edinburgh El Tercih Anketi, bireylere günlük yaşam aktivitelerinde el kullanımlarını sorgulayan geçerli ve güvenilir bir ankettir. Anketin uygulamasında bireylere on farklı aktivite (yazı yazma, diş fırçalama, makas kullanma gibi) sırasında el kullanımlarına yönelik sorular sorulur (11). Dominant tarafı bilateral olan katılımcılarda yay ve kiriş kolunun stabil taraflar olup olmadığı saptandı. Buna göre kiriş ve yay kolu bu bireylerde belirlendi.

### **Eklem mobilitesinden değerlendirilmesi:**

Carter ve Wilkinson tarafından geliştirilen standart protokolün Beighton tarafından modifiye edilmiş şekli ile değerlendirildi. Beighton puanı 5 ve üstü olan bireylerin, eklem hipermobilitésine sahip oldukları kabul edildi (12,13).

### **Kas gücünün değerlendirilmesi:**

Katılımcıların her iki üst ekstremitesindeki m. biceps brachii ve m. triceps brachii kasları Hand-Held Dinamometresin (BIODEX, Biodex system 3, Biodex Medical System Corp., NY, USA) kullanılarak ölçüldü. Ölçümler katılımcı her iki ayağa eşit ağırlık verdiği ayaklar omuz hizasında açık olduğu ayakta dik pozisyonda, omuz ve dirsek 90° fleksiyonda, ön kol supinasyonda iken maksimum izometrik istemli kontraksiyonlar şeklinde ölçülerek elde edildi. Sonuç kg/Newton cinsinden kaydedildi. Her bir kas testi 3'er kez tekrarlandı (10 saniye kontraksiyon, 30 saniye dinlenme) ve ölçümlerin ortalamaları alındı. Test sırasında kuvvet kompensasyonu açısından gövde fleksiyonuna izin verilmedi. Geçerlilik ve güvenilirliği yüksek olan, altın standart kabul edilen hidrolik el dinamometresi (Saehan Corp. Korea) el kavrama ölçümlerinde kullanıldı. Benzer çalışmalarda ki gibi; ayakta dik pozisyonda, ayaklar omuz hizasında açık şekilde, omuz adduksiyon, dirsek 90° fleksiyonda, ön kol nötralde ölçümler yapıldı. Her iki ekstremité ölçümleri 20 sn ara verilerek 3 kez tekrarlandı. Veriler kilogram cinsinden kaydedildi ve ortalamaları alındı (14). Baseline Hydraulic Pinch Gauge ölçüm cihazı (kg cinsinden) kullanılarak baş parmak pink kuvveti 3 kez (10 saniye kontraksiyon, 30 saniye dinlenme) ile ölçüldü ve ortalamaları değerlendirmelere dahil edildi.

### **Reaksiyon zamanının değerlendirilmesi:**

Reaksiyon zamanı için Nelsonun ölçümü kullanılmıştır. Bu ölçüm şu şekilde yapılmaktadır; ölçümü yapılacak kişi sandalyede oturur. Omuz nötral pozisyonda, kol gövde yanında, dirsek 90° fleksiyonda, ön kol nötral pozisyonda olacak şekilde kol pozisyonlanır. Baş parmak ve diğer 4 parmak aralığından geçecek şekilde cetvel bırakılır. Bırakılan cetvelin başparmak ve işaret parmak arasında tutulması istenir. Cetvelin tutulduğu başparmak altındaki değer cm cinsinden kaydedilir. 3 uygulaması yapılır ve ortalaması alınır. Reaksiyon zamanı için; Reaksiyon Zamanı= $\sqrt{2 \times \text{Cetvelin düştüğü mesafe/yer çekimine bağlı hız}}$  (Reaksiyon zamanı= $\sqrt{2 \times \text{Mesafe (cm) / 980 msn}}$ ) olarak hesaplanır (15). Çalışmada belirtilen formülasyon yerine başparmağın altındaki değer reaksiyon zamanı olarak değerlendirildi.

Verilerin istatistiksel değerlendirmesi, SPSS 20.0 istatistik paket programı kullanılarak yapıldı. Nicel

**Tablo 1.** Grupların demografik özelliklerinin gösterimi.

	<b>Grup 1</b> <b>n= 10</b> <b>(Ort±SS)</b>	<b>Grup 2</b> <b>n= 12</b> <b>(Ort±SS)</b>	<b>Grup 3</b> <b>n= 12</b> <b>(Ort±SS)</b>	<b>Toplam</b> <b>n= 34</b> <b>(Ort±SS)</b>
Yaş (yıl)	24.60±2.59	25.00±1.99	22.66±1.18	23.11±1.06
(min-mak)	(18.00- 28.00)	(18.00-29.00)	(19.00-24.00)	(18.00-29.00)
Boy (cm)	176.60±11.57	168.41±11.54	162.66±6.82	168.79 ±11.34
Kilo (Kg)	69.25±14.43	64.50±18.12	53.83±9.95	62.13±15.54
DT	Bilateral:3 Sol:1-Sağ:6	Bilateral:1 Sol:0-Sağ:11	Bilateral:4 Sol:0-Sağ:8	Bilateral:8 Sol:1-Sağ:25

DT: Dominant taraf, n: kişi sayısı

veriler için tanımlayıcı istatistikler; ortalama ± standart sapma (SS), minimum ve maksimum değerler olarak ifade edilirdi. Normalite incelemesi için Kolmogorov-Smirnov Testi kullanıldı. Verilerin normal dağılıma uygun olduğu görüldü. Yapılan homojenlik testi sonucunda Sig. (Anlamlılık) sütunundaki değerlerin 0,05'den büyük olması incelenen faktörlerin dağılımlarının homojen olduğunu gösterdi.

Grup içi kiriş ve yay kolu verilerinin karşılaştırılması Paired Samples Test ile yapılmıştır. Gruplar arası verilerin farklılığı Oneway anova testi ile değerlendirildi. Bu testin ileri aşamasında ise farkın hangi gruplardan kaynaklandığını görebilmek adına Post-Hock testlerden Tukey kullanıldı. Anlamlılık düzeyi  $p<0,05$  olarak alındı.

Araştırmanın sorusu; tek sporda ve aynı anda yapılan eksantrik antreman ile konsantrik antremanın oluşturduğu güç kazanımı üstünlüğü hangi egzersiz türünde daha fazladır?

## BULGULAR

Çalışma sonunda elde edilen verilere göre grupların yaş, boy, kiloları (Ort. ±SS) Tablo 1. de verilmiştir. Demografik sorguda elit sporcu seviyesinde

olan (Grup 1) 1 sporcunun yayı sağ eliyle tuttuğu kaydedildi, bunun dışında tüm sporcuların yayı sol eli ile kavradıkları, kirişi de sağ eli ile tuttukları belirlendi. Yapılan "Edinburg El Tercihi Anketi" Değerlendirmesi sonucunda skor hesaplarına göre 8 bireyin bilateral dominant olduğu, 1 bireyin sol dominant, 25 bireyin ise sağ dominant olduğu saptanmıştır. Bilateral dominant olan bireylerde kiriş ve yay kolu uygulamalı olarak gözlemlendi ve sağ dominant kişilerle aynı yay ve kiriş kolunu kullandıkları belirlenerek veriler buna uygun kaydedildi (Tablo 1).

Gruplarda ölçülen parametrelerin gruplara göre ortalama ± standart sapma (SS), Tablo 2 de gösterildi. Buna göre spor yapmayanlarda kiriş kolunda yani dominant kolda yapılan ölçümler sonucunda daha yüksek değerler elde edildi. Spor düzeyi arttıkça değişkenlikler dikkat çekti. M. biceps brachii ve m. triceps brachii kas gücü eksantrik kasılma yönünde yüksek olarak belirlendi.

Grup içi kiriş ve yay kolu verilerinin karşılaştırılması Paired Samples Test ile yapılmıştır. Anlamlılık düzeyi  $p<0.05$  olarak alınmıştır. Grup içi yapılan analizde elit okçularda (grup 1) m. biceps brachii ve m. triceps brachii kas gücünde, başlangıç düzeyindeki

**Tablo 2.** Grup içi parametre sonuçları

<b>Ölçülen Parametreler</b>	<b>Grup 1</b> <b>(Ort±SS)</b>	<b>Grup 2</b> <b>(Ort±SS)</b>	<b>Grup 3</b> <b>(Ort±SS)</b>
KBG (kg/N)	24.12±6.23	22.46±9.75	18.52±7.25
YBG(kg/N)	26.15±6.51	21.97±10.90	17.00±6.71
KTG (kg)	20.06±6.26	17.66±6.28	13.38±3.47
YTG( kg)	18.92±5.11	16.74±5.42	12.50±3.95
KEKG (kg)	15.19±6.16	14.72±5.48	10.61±4.20
YEKG (kg)	15.16±5.83	13.11±5.39	09.16±3.95
KPG(kg)	7.95±2.54	7.35±2.46	5.34±1.17
YPG(kg)	7.80±2.36	7.06±2.13	4.02±1.11
KRH	13.76±3.55	14.91±2.84	11.75±3.53
YRH	13.93±3.09	14.58±4.06	10.79±2.24

KBG: kiriş m. biceps brachii gücü; KEKG: kiriş el kavrama gücü, KPG: kiriş pinç gücü; KRH: kiriş reaksiyon hızı; KTG: Kiriş m. ticeps brachii gücü ; YBG: yay m. biceps brachii gücü; YEKG: yay el kavrama gücü; YPG: yay pinç gücü; YRH: yay reaksiyon hızı, YTG: yay m. ticeps brachii gücü

**Tablo 3.** Grup içi kiriş ve yay kolları arasındaki farkın sonuçları

Grup	ORT.	SS	Sig. (2-tailed)
Grup 1 n= 10			
KBG-YBG	2.033	1.680	0.004*
KTG-YTG	-0.143	2.120	0.011*
KEKG-YEKG	0.031	1.651	0.954
KPG-YPG	0.148	0.910	0.620
KRH-YRH	-0.165	3.119	0.871
Grup 2 n= 12			
KBG-YBG	0.495	3.165	0.599
KTG-YTG	0.922	1.208	0.023*
KEKG-YEKG	0.610	0.863	0.032*
KPG-YPG	0.291	0.965	0.318
KRH-YRH	0.334	3.552	0.751
Grup 3 n= 12			
SağBG-solBG	0.519	2.723	0.023*
sağTG-solTG	-0.120	1.331	0.045*
sağEKG-solEKG	0.445	1.173	0.041*
sağPG-solPG	0.314	0.492	0.049*
sağRH-solRH	0.959	3.229	0.326

\* Paired Samples Test/Anlamlılık düzeyi p&lt;0.05

KBG: kiriş m. biceps brachii gücü; KEKG: Kiriş el kavrama gücü, KPG: Kiriş pinç gücü, KTG: kiriş m. ticeps brachii gücü, PG: pinç gücü, RH: reaksiyon hızı, TG: m. ticeps brachii gücü, YBG: Yay m. biceps brachii gücü, YEKG: Yay el kavrama gücü, YPG: yay pinç gücü; KRH: Kiriş reaksiyon hızı; YRH: yay reaksiyon hızı, YTG: yay m. ticeps brachii gücü

**Tablo 4.** Verilerin gruplararası karşılaştırma sonuçları

Grup	Karşılaştırmalı grup	ORT.	SS	Sig.	
Sağ BG	1	2	3.68800	3.44683	0.539
		3	7.62883	3.44683	0.035*
	2	3	3.94083	3.28642	0.463
Sol BG	1	2	2.15000	3.56893	0.820
		3	6.11500	3.56893	0.036*
	2	3	3.96500	3.40284	0.482
Sağ TG	1	2	2.25483	2.17924	0.561
		3	6.54067*	2.17924	0.014*
	2	3	4.28583	2.07783	0.114
Sol TG	1	2	3.32033	2.24144	0.314
		3	6.56283*	2.24144	0.017*
	2	3	3.24250	2.13713	0.297
Sağ EKG	1	2	0.47633	2.26491	0.976
		3	4.58633	2.26491	0.123
	2	3	4.11000	2.15951	0.155
Sol EKG	1	2	1.05617	2.17282	0.878
		3	5.00033	2.17282	0.071
	2	3	3.94417	2.07170	0.155
Sağ PG	1	2	0.60050	.91002	0.788
		3	2.61133*	.91002	0.020*
	2	3	2.01083	.86767	0.068
Sol PG	1	2	0.74417	.82287	0.642
		3	2.77750*	.82287	0.006*
	2	3	2.03333*	.78457	0.037*
Sağ RH	1	2	-1.14950	1.41825	0.699
		3	2.01717	1.41825	0.042*
	2	3	3.16667	1.35225	0.065
Sol RH	1	2	-.65033	1.38222	0.886
		3	3.14133	1.38222	0.035*
	2	3	3.79167*	1.31789	0.019*

\* Oneway anova devamında post-hock olarak Tukey testi yapılmış olup, anlamlı olan gruplar arası sonuçlar bold olarak işaretlenmiş ve tek tabloda birleştirilmiştir.

\*\*Anlamlılık düzeyi p&lt;0.05

BG: m. biceps brachii gücü, EKG: el kavrama gücü, PG: pinç gücü, RH: reaksiyon hızı, TG: m. ticeps brachii gücü

okçularda (grup 2) m. triceps brachii ve el kavrama güçlerinde, spor yapmayan bireylerde (grup 3) ise tüm ölçümlerde kiriş ve yay kolları arasında anlamlı farklılık tespit edildi (Tablo 3).

Değerlendirilen tüm verilerin gruplara göre karşılaştırılmasının analizinde profesyonel okçuların yay kolu verileri sol, kiriş kolu verileri sağ üst ekstremitede olarak değerlendirilirken, sadece 1 sporcu için dominant taraf sol olması sebebiyle bu sporcunun verileri tam tersi olarak yay kolu sağ, kiriş kolu sol olarak değerlendirmeye dahil edilerek istatistiksel hesaplamalar yapılmıştır.

Tüm ölçüler parametreler gruplara göre karşılaştırıldığında; grup 1 ve grup 3 arasında tüm parametrelerde hem sağ hem de sol ekstremitede anlamlı farklılık belirlendi. Grup 2 ve grup 3 arasında ise sol pinç gücü ve sol reaksiyon hızında anlamlı fark tespit edildi. Grup 1 ve grup 2 arasında hiçbir parametrede anlamlı fark bulunmadı (Tablo 4).

## TARTIŞMA

İzotonik egzersiz tipleri arasındaki üstünlük hem spor branşlarında hem de tedavi protokollerinde önem kazanmıştır. Bu bakımdan son yıllarda bu konu üzerinde çalışmalar artmaktadır. Kasın mimari yapısında egzersiz tipinin etkisinin farklılık gösterdiğini bildiren çalışmalar; eksantrik kasılma sonrasında bazı sarkomerlerin normal fizyolojik yerleşimini geri kazanmadığını, özellikle tekrarlayan güçlü eksantrik kasılmalardan sonra geri dönüşümü olmayan fiber membran yırtıkları, kontrolsüz Ca<sup>2+</sup> hareketliliği, doku içi kanama gibi sorunların yaşandığını belirterek spor branşlarında karşılaşılan yaralanma farklılıklarına egzersiz tipinin etkisine işaret etmişlerdir (5,16-18).

Yapılan çalışmalar eksantrik kasılmanın daha çok kas yorgunluğuna sebep olduğunu bildirmiştir. Bu durumda da kas gücünün olumsuz etkilendiği ifade edilmektedir (19). Ancak literatürde kas performansı konusunda egzersiz tipinin üstünlüğü hakkında çelişkiler vardır. Bazı araştırmacılar eksantrik eğitimlerin konsantrik eğitiminden daha fazla kas hipertrofisine ve nöral aktivasyon artışına sebep olduğu bildirmişlerdir (20-22). Ayrıca; rehabilitasyon yaklaşımlarında eksantrik egzersizlerin tedavide güç, tork ve ağrı üzerinde çok daha avantajlı olduğu belirtilmiştir (23).

M. biceps brachii kasında eksantrik odaklı güç egzersizlerin başlangıç düzeyindeki sporcularda konsantrik odaklı güç egzersizlerine göre güç kazanımı açısından hiçbir fark olmadığını gösteren çalışmalara benzer (7) sonuç elde edilmişken, uzun süredir

antreman yapan elit sporcularda eksantrik direnç eğitiminden sonra üstün güç kazanımlarının elde edildiğini belirten araştırmalar (24) desteklenmiştir. M. triceps brachii kasının eksantrik ve konsantrik odaklı dirençli egzersizlerle gücünün arttığı, ancak dominant tarafın bu sporda eksantrik güç gerektirmesi sebebiyle her seviyedeki sporcuda eksantrik kasılan dominant taraf daha güçlü olarak değerlendirilmiştir. Bu bulgu dominant ekstremitenin tüm sporcularda daha güçlü olmasıyla açıklanabilir.

Kısa süreli güçlendirme çalışmalarında izotonik egzersiz tipinin kas gücü ve hipertrofi üzerinde üstünlüğünün olmadığı belirlenmiştir çalışmalar vardır (25,26), benzer şekilde bizim çalışmamızda da başlangıç seviyesindeki sporcularda m. biceps brachii kasında güç kazanımında egzersiz tipinin etkisi anlamlı bulunmadı. Uzun süreli antreman çalışmalarında ise eksantrik odaklı direnç egzersizlerinin hem güç, hem hipertrofi hem de tendon sorunu olan vakalarda ağrı üzerinde olumlu etkisi belirtilmiştir (23, 27).

Vincent ve ark. (22) eksantrik egzersizlerin cinsiyete göre kasın mimari yapısında değişikliklere yol açtığını belirtmişlerdir. Çalışmamızın en önemli sınırlaması cinsiyet faktörünün değerlendirilmemiş olmasıdır. Gelecekteki çalışmalarda cinsiyetin egzersiz tipi üzerindeki etkinliğinin değerlendirilmesi dikkate alınmalıdır. Ayrıca beklentilerimizin aksine çalışmaya gönüllü olan tüm sporcular yaşadıkları sakatlıklar sebebiyle çalışmaya dahil edilemediği için katılımcı sayısı beklenenin altında kalmıştır. Ancak gruplarda yaş ortalamasının yakın olması gruplar arası homojeniteyi sağlamıştır. Bu çalışmanın bir başka sınırlılığı ise kas hipertrofisinin egzersiz tipine göre değişkenliğinin ölçülemediği olmasıdır. Bu açıdan başka çalışmalarda aynı birey üzerinde bu değişkeninde ölçülmesinin faydalı olacağına inanıyoruz. Çalışmanın güçlü yönü ise aynı bireyde aynı anda her iki direnç odaklı egzersiz tipinin değerlendirilmiş olmasıdır. Böylece bireysel farklılıklardan doğabilecek sapmalar ve zamansal değişkenliklerden dolayı performans değişiklikleri en aza indirgenmiş oldu.

Bu çalışmada okçuluk spor düzeyi arttıkça sağ ve sol taraf parmak, kavrama kas güçlerindeki farklılığın giderek azaldığı belirlenmiştir. Ancak spor düzeyi arttıkça yay kolundaki m. biceps brachii, kiriş kolunda ise m. triceps brachii'nin kas gücünde anlamlı artışı dikkat çekmektedir. Bu durum bize uzun süreli eksantrik egzersizin, konsantrik egzersize göre m. biceps brachii ve m. triceps brachii kaslarının gücünü daha fazla arttırdığını düşündürür. Çünkü bu sporda

eksantrik egzersizin yay kolunda m. biceps brachii'yi giriş kolunda da m. triceps brachii'yi geliştirdiği bilinmektedir. Okçuluk sporunda yapılan her iki tip egzersizinde m. biceps brachii, m. triceps brachii, pinç güçlerini artırdığı ve reaksiyon hızlarını geliştirdiği bulunmuştur. Ancak eksantrik odaklı dirençli egzersizlerin m. biceps brachii ve m. triceps brachii kaslarının performansını konsantrik odaklı dirençli egzersizlere göre daha fazla artırdığı belirlenmiştir.

Kısa süreli yapılan çalışmalarda izotonik egzersizlerin kas gücü ve kas hipertrofisi üzerinde etkileri konusunda farklı sonuçlar rapor edilmiştir. Fakat; bu çalışma sonuçlarına göre kas gücü üzerinde eksantrik odaklı dirençli egzersizin üstün olduğu tespit edilmiştir.

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# Opioid Kullanım Bozukluklu Bireylerde Algılanan Sosyal Desteğin Remisyon Süresiyle İlişkisi

## *The Relationship between Perceived Social Support and Duration of Remission in Individuals with Opioid Use Disorder*

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### Öz

**Amaç:** Bu çalışmanın amacı opioid kullanım bozukluğu (OpKB) olan bireylerde algılanan sosyal destek düzeyi ile remisyon süresi arasındaki ilişkiyi araştırmaktır.

**Hastalar ve Yöntem:** Araştırmaya alkol ve madde bağımlılığı tedavi merkezleri (AMATEM) polikliniğine Ağustos-Kasım 2020 tarihlerinde başvuran OpKB tanısı olan 199 kişi dahil edildi. En az 1 yıldır remisyonunda olan 90 kişi uzun remisyon (UR) grubu, remisyon süresi 1 yıldan kısa olan 109 kişi kısa remisyon (KR) grubu olarak kabul edildi. Ölçüm araçları olarak sosyodemografik veri anketi ile Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ) kullanıldı.

**Bulgular:** UR ve KR grupları arasında ÇBASDÖ skorları açısından istatistiksel olarak anlamlı bir fark saptanmadı ( $p>0.05$ ). UR grubunun KR grubuna göre daha çok şehirde yaşadığı ( $p=0.034$ ) ve kuruluk döneminde daha çok ilaç tedavisi kullandığı ( $p<0.001$ ) bulundu.

**Sonuç:** OpKB olan kişilerin kuruluk döneminde ilaç tedavisi alıyor olmaları remisyon sürelerine olumlu katkı sağlamaktadır. Şehirde yaşıyor olmanın OpKB olan kişilerin remisyon süresi ile olumlu bu ilişkisi olduğu, bunun yanında kişilerin algıladıkları sosyal destek düzeylerinin remisyon kalma süresi ile anlamlı bir ilişki olmadığı söylenebilir.

**Anahtar Kelimeler:** Opioid kullanım bozukluğu, algılanan sosyal destek, remisyon, ilaç tedavisi

### Abstract

**Aim:** The primary objective of this investigation is to examine the relationship between individuals' perceived levels of social support and the duration of remission among those diagnosed with opioid use disorder (OpUD).

**Patients and Methods:** 199 people with a diagnosis of OpUD who applied to the AMATEM outpatient clinic between August and November 2020 were included in the study. 90 people who were in remission for at least 1 year were accepted as the long remission (LR) group, and 109 people with a remission period of less than 1 year were considered as the short remission (SR) group. The sociodemographic questionnaire and Multidimensional Scale of Perceived Social Support (MSPSS) were utilized as measurement instruments.

**Results:** When the LR and SR groups were compared in terms of duration of the remission, no statistically significant difference was found between MSPSS scores ( $p>0.05$ ). It was found that the LR group lived more in the city than the SR group ( $p=0.034$ ) and used more drug treatment during the dryness period ( $p<0.001$ ).

**Conclusion:** The administration of medication to individuals with OpUD during the abstinence phase positively influences the duration of the remission period. Additionally, it can be suggested that urban residency is associated with an extended remission duration among individuals with OpUD. Conversely, the perceived levels of social support within the sample do not exhibit a statistically significant correlation with the duration of remission.

**Key words:** Opioid use disorder, perceived social support, remission, medical treatment.

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**Açıklama:** Yazarların hiçbirisi, bu makalede bahsedilen herhangi bir ürün, aygıt veya ilaç ile ilgili maddi çıkar ilişkisine sahip değildir. Araştırma, herhangi bir dış organizasyon tarafından desteklenmedi. Yazarlar çalışmanın birincil verilerine tam erişim izni vermek ve derginin talep ettiği takdirde verileri incelemesine izin vermeyi kabul etmektedirler.



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## GİRİŞ

Tüm dünyada olduğu gibi ülkemizde de madde kullanım bozukluğu ve davranışsal bağımlılıklar insan gelişimini ve toplumsal sağlığı tehdit eden, önlenemez yükselişi ile korkutucu boyutlara ulaşarak felaketlere yol açması an meselesi olan bir halk sağlığı sorunudur. Opioidler, toplumumuzda en çok bilinen ve korkulan, kaçınılması gerektiği düşünülen maddelerden biridir. Bu yüzden, toplumun bu tehditleri kolay anlaması bakımından opioid kullanım bozukluğu (OpKB) bilimsel arenada olduğu kadar halkı bilgilendirme konusunda da öne çıkması gerektiği düşünülen bir grup madde kullanım bozukluğudur. Avrupa Uyuşturucu ve Uyuşturucu Bağımlılığı İzleme Merkezi (EMCDDA)'nin yayınladığı raporda, Avrupa'da bir milyon yüksek riskli opioid kullanıcısının olduğu, bağımlılık tedavisi için başvuruların %28'inin opioid kullandığı, ölüm sebebi yüksek doz olan bağımlıların ise %74'ünün opioid kullanıcısı olduğu belirtilmektedir (1).

Opioid kullanım bozukluğu, kronik bir psikiyatrik rahatsızlık olup remisyon ve relaps dönemlerini içerir (2-4). Bu bozukluğu tanımlarken psikiyatrik literatürde bozukluk (disorder) kelimesi ile açıklanması uygun görülmesine rağmen bu durumun tıbbi bedensel bir hastalık (disease) olarak seyrettiği mutlaka vurgulanmalıdır. Bu bozukluğun, ortaya çıkması ve seyrine önemli katkılar sağlayan ciddi psikolojik, sosyal ve biyolojik risk faktörleri vardır. Bunlar ayrıca remisyon süresi ve relaps riskini de belirleyen faktörlerdir (4). Başlıcaları; medeni durum, sosyoekonomik düzey, yaş, nöropsikolojik bozulma, bağımlılığın şiddeti, maddenin cinsi, bireyin sosyal destekleri gibi faktörlerdir (3-7).

Sosyal destek; kişinin ihtiyaç duyduğu zamanda, ailesi, arkadaşı, eşi ya da profesyonel bir kişiden sağladığı bilişsel, duygusal veya maddi destektir. Yapılan araştırmalar, yetersiz sosyal desteğin psikiyatrik semptomların artışına neden olabileceğini göstermektedir (8,9). Çalışmalarda; Sosyal destek algısının yüksek olduğu bireylerin madde kullanımını azaltma konusunda daha başarılı oldukları ve bağımlılık tedavisine daha olumlu yaklaştıkları bulunmuştur (9,10).

Literatürde sosyal desteğin iki bileşeninden söz edilmektedir (11). Bunlardan yapısal bileşen, sosyal ağın niteliksel özelliklerini yani sağlanan (objektif) sosyal desteği içerirken, işlevsel bileşen ise algılanan (subjektif) destek düzeyini ifade eder (12,13). Sağlanan sosyal destek, destek kaynaklarından sağlanan sosyal destek miktarı ve

desteğin davranışsal değerlendirilmesi olarak kabul edilir. Algılanan sosyal destek ise, bireyin diğerleriyle kuvvetli bağları olduğuna inanması ve destek sağlayacağına ilişkin kişisel bilişsel algılamasıdır (5). Gerçekte hem sağlanan hem algılanan destek sosyal ve ruhsal, hatta bedensel iyilik ile ilişkilidir. Bazı çalışmalar; algılanan sosyal desteğin kişilerin yaşam kalitelerinin artmasında, stresli yaşam olaylarıyla başa çıkmalarında ve problem çözme becerilerinde olumlu etkilerinin olduğunu göstermektedir (5,14,15). Aile desteği, finansal destek gibi objektif destekleyici yaklaşımların alkol ve madde kullanım bozuklukları ile ilişkisi çalışılmış olmasına rağmen (9,10,16), algılanan sosyal desteğin bu kişilerde yaşam kalitesi ve hastalığın seyri üzerine olumlu etkileri olduğuna dair az sayıda çalışma olduğu ve özellikle OpKB olan kişilerde yapılacak yeni çalışmalara ihtiyaç duyulduğu göze çarpmaktadır (6,17-20). Hâlbuki; toplumumuzda alkol kötüye kullanımı ve opioid kötüye kullanımı arasında bireysel ve toplumsal kabullenme ve damgalama konusunda ciddi farklılıklar görülmekte, destek sağlama açısından da ayırıcılık olabileceği düşünülmektedir (21,22)

Bildiğimiz kadarıyla sadece OpKB olan kişilerde algılanan sosyal desteğin remisyon süresi üzerine olan etkilerine dair kısıtlı sayıda çalışma vardır (19). Biz bu çalışmada çoklu madde ve alkol kullanım bozukluğu olmayıp sadece opiyat kullanım bozukluğu olan kişilerde algılanan sosyal destek düzeyinin remisyonunda kalma süresi üzerine olan etkilerini araştırmayı amaçladık.

## HASTALAR VE YÖNTEM

### a. Örneklem:

Çalışmamıza Dr. Abdurrahman Yurtaslan Ankara Onkoloji Eğitim ve Araştırma Hastanesi Eğitim Araştırma Hastanesi Alkol ve Madde Tedavi Merkezi (AMATEM) polikliniğine Ağustos-Kasım 2020 tarihlerinde ayaktan başvuran Mental Bozuklukların Tanısal ve Sayımsal Elkitabı (DSM-5) tanı ölçütlerine göre daha önceden Opiyat Kullanım Bozukluğu tanısı olan hastalar alındı. DSM-5'te "erken remisyon, 12 aydan kısa süreli remisyon" ve "kalıcı remisyon, 12 ay veya daha uzun süreli remisyon" olarak tanımlanmış remisyon gidişleri göz önünde bulundurularak katılımcılar 2 gruba ayrıldı; bunlardan 90'ı en az 1 yıldır remisyonunda olan bireylerden, 109'u ise 1 yıldan kısa süre içinde relaps olan bireylerden oluşmuştu. 1 yıldan kısa remisyon süresi olanlar kısa remisyon grubu (KR), 1 yıldan uzun remisyon süresi olanlar uzun remisyon grubu (UR) olarak adlandırıldı. Dahil

edilme ölçütlerini karşılayan bireyler çalışma hakkında bilgilendirilerek yazılı katılım onayları alındı. Katılmaya gönüllü olan 210 kişiye ayrıntılı sosyodemografik veri anketi ve Çok Boyutlu Algılanan Sosyal Destek Ölçeği uygulandı. Ölçek sorularını tam yanıtlamayan 11 kişi analizlere dahil edilmedi. Dr. Abdurrahman Yurtaslan Ankara Onkoloji Eğitim ve Araştırma Hastanesi'nden 26/08/2020 tarih ve 2020-08/758 sayılı etik kurul onamı alınmıştır.

### b. Değerlendirme araçları:

#### i. Sosyodemografik ve Klinik Veri Formu

Çalışmaya dahil edilen hastaların demografik bilgilerini toplamak amacıyla araştırmacılar tarafından oluşturulmuş anket formudur. Bu form, hastaların yaşı, eğitimi, mesleği gibi kişisel bilgilerin yanında hastalıkla ilgili; hastalığın başlangıç yaşı, yatış sayısı, relaps sayısı, remisyonunda kalma süresi gibi bilgileri içermektedir.

#### ii. Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ASDÖ)

Toplam 12 maddeden oluşan ölçek, dörder maddeden oluşan ve desteğin kimden geldiğini ifade eden 3 gruba (aile, arkadaş ve özel bir insan (diğer)) bölünmüştür. Zimet ve ark. tarafından 1988'de geliştirilen ölçeğin Türkçe geçerlik ve güvenilirliği 2001'de Eker ve ark. (23,24) tarafından yapılmıştır. Artan puanlar algılanan sosyal desteğin arttığını, azalan puanlar algılanan sosyal desteğin azaldığını ifade etmektedir.

### c. İstatistiksel Analiz:

Verilerin analizi SPSS 15.0 paket programıyla yapılmıştır. Verilerin tanımlanmasında sayı, yüzde, ortalaması±standart sapma, ortanca, minimum ve maksimum değerleri kullanılmıştır. Sürekli değişkenlerin normal dağılıma uygunluğu Kolmogorov Smirnov testi ile değerlendirilmiştir. Gruplar arası karşılaştırmalarda kategorik değişkenler için ki kare testi kullanılmıştır. Sürekli değişkenler için student t testi veya mann whitney u testi kullanılmıştır. Değişkenler arası doğrusal ilişki pearson korelasyon testi ile yapılmıştır. P <0.05 düzeyi istatistiksel olarak anlamlı kabul edilmiştir.

### BULGULAR

Çalışmaya dahil edilen toplam 199 kişiye ait yaş ortalaması 28,2±6,2 yıl (en küçük =18, en büyük=63) idi. KR grubu 109, UR grubu 90 kişiden oluşmaktaydı. KR (27,5±5,2 yıl) ve UR (29,0±7,3 yıl) gruplarının yaş ortalamaları açısından istatistiksel olarak anlamlı fark saptanmadı. Grupların sosyodemografik yönden karşılaştırılması Tablo 1'de sunulmuştur. Gruplar arasında "yaşanılan yer" yönünden istatistiksel olarak anlamlı bir fark varken (p=0.034), diğer sosyodemografik özellikler yönünden gruplar arasında istatistiksel olarak anlamlı bir fark yoktu (p>0.05).

Gruplar, kurulum döneminde idame tedavide ilaç (opioid agonist veya antagonisti) kullanımı yönünden istatistiksel olarak anlamlı farklılık gösteriyordu

**Tablo 1.** KR ve UR gruplarının sosyodemografik yönden karşılaştırılması

Değişken		KR n=109 n (%)	UR n=90 n (%)	P*
Cinsiyet	Erkek	105 (96,3)	81 (90)	0.072
	Kadın	4 (3,7)	9 (10)	
Eğitim	Ortaöğretim ve altı	47 (49,0)	42 (51,2)	0.762
	Lise	45 (46,9)	35 (42,7)	
	Üniversite	4 (4,2)	5 (6,1)	
Düzenli İş	Var	68 (62,4)	61 (67,8)	0.428
	Yok	41(37,6)	26 (32,2)	
Sosyal Güvence	Var	79 (73,1)	68 (76,4)	0.601
	Yok	29 (26,9)	21 (23,6)	
Medeni Durum	Evli	29 (26,6)	30 (33,3)	0.529
	Bekâr	73 (67,0)	56 (62,2)	
	Boşanmış/Dul	7 (6,4)	4 (4,4)	
Aylık Gelir (TL)	1000 ve altı	53 (56,4)	46 (55,4)	0.096
	1000 – 3000	36 (38,3)	25 (30,1)	
	3000 ve üzeri	5 (5,3)	12 (14,5)	
Yaşadığı Yer	İl	51 (48,1)	59 (66,3)	0.034
	İlçe	48 (45,3)	27 (30,3)	
	Köy	7 (6,6)	3 (3,4)	
Yaş	Ort.±SS (yıl) (min-max)	27,5±5,2 (18 – 45)	29,0±7,3 (18 – 63)	0.311**

KR: Kısa Remisyon, UR: Uzun Remisyon, \* Ki kare testi

\*\* Mann Whitney U testi

**Tablo 2.** Grupların madde kullanım özellikleri yönünden karşılaştırılması

Değişken		KR n=109 n (%)	UR n=90 n (%)	P*
Ailede Madde Kullanımı	Evet	19 (17,6)	14 (17,1)	0.925
	Hayır	89 (82,4)	68 (82,9)	
iv Opiyat Kullanımı	Evet	23 (21,3)	23 (25,6)	0.480
	Hayır	85 (78,7)	67 (74,4)	
Kuruluk Döneminde İlaç Kullanımı	Evet	78 (71,6)	84 (93,3)	<0.001
	Hayır	31 (28,4)	6 (6,7)	
Cezaevi Öyküsü	Evet	27 (25,0)	17 (19,1)	0.323
	Hayır	81 (75,0)	72 (80,9)	
Maddeye Başlama Yaşı	Ort.±SS (yıl) (min-max)	17,4±3,8 (10-31)	18,2±5,4 (11-43)	0.865**
İlk Opiyat Kullanım Yaşı	Ort.±SS (yıl) (min-max)	21,0±4,5 (14-41)	21,1±5,7 (14-43)	0.535**
Toplam Opiyat Kullanım Süresi	Ort.±SS (ay) (min-max)	58,5±36,2 (2-132)	61,0±44,9 (3-300)	0.845**

KR: Kısa Remisyon, UR: Uzun Remisyon, \* Ki kare testi \*\* Mann Whitney U testi

**Tablo 3.** Grupların Algılanan Sosyal Destek (ASD) Ölçek Puanları Yönünden Karşılaştırılması.

Değişkenler	KR Ortalama ±SS	UR Ortalama ±SS	P*
ASD Aile	22,7±6,8	23,5±6,7	0.407
ASD Arkadaş	13,6±7,9	13,6±7,7	0.984
ASD diğer	16,0±8,6	16,8 ±8,6	0.538
ASD Toplam	52,5±17,7	54,0±17,3	0.536 **

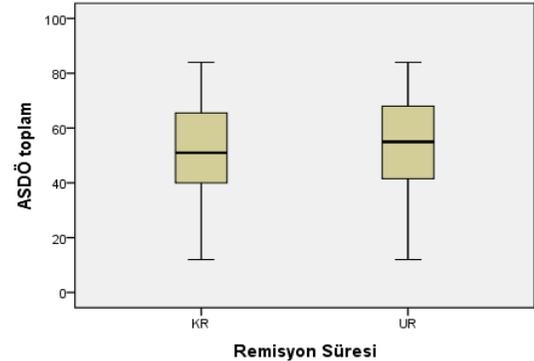
KR: Kısa Remisyon, UR: Uzun Remisyon, SS: Standart sapma, ASD: Algılanan Sosyal Destek, \* Mann Whitney U testi \*\* student t testi

( $p < 0.001$ ). UR grubunda düzenli agonist ya da antagonist ilaç kullanan hasta sayısı KR grubundan daha fazlaydı. Grupların madde kullanım özellikleri yönünden karşılaştırılması Tablo 2'de sunulmuştur. İki grubun ASDÖ ve alt ölçek skorları arasında istatistiksel olarak anlamlı bir fark bulunmadı ( $p > 0.05$ ). Grupların ASDÖ skorları Tablo 3'de verildi.

Örneklem UR ve KR grubu olarak ikiye ayrılırken aynı grup içindeki dağılım farkından dolayı (Ör: KR grubunda 1 aydır ve 11 aydır remisyonunda olan kişiler olması), tüm örneklemin remisyon süreleri ay olarak hesaplanmış ve ÇBASDÖ toplam puanı, sosyodemografik ve klinik özellikleri ile ilişkisi değerlendirilmiştir. Yapılan Pearson korelasyon analizinde; ÇBASDÖ toplam puanı ile örneklemin remisyon süresi arasında istatistiksel olarak anlamlı bir ilişki saptanmamıştır ( $p = 0,363$ ,  $r = 0,064$ ). Grupların ASDÖ toplam puanlarına ait boxplot analizi Grafik 1 de gösterilmiştir" yazılacak. grafiğin üstüne de: " Şekil 1. Grupların ASDÖ puanlarının boxplot analizi

## TARTIŞMA

Çalışmamızın sonuçları, algılanan sosyal destekle

**Şekil 1.** İki grup için ASDÖ toplam puanı

remisyonunda kalma süresi arasında istatistiksel olarak anlamlı bir ilişki olmadığını göstermiştir. Algılanan sosyal desteğin pek çok ruhsal ve bedensel bozukluğun ortaya çıkışında, tedavisinde, seyrinde ve prognozunda etkili olduğunu, yeterli sosyal desteğin kişilerde bu parametrelere olumlu katkı sağlayacağı araştırmalarda ortaya konulmuştur (25–27). Algılanan

sosyal destekteki yetersizliğin depresyon, bipolar bozukluk, psikoz ve anksiyete bozuklukları gibi psikiyatrik bozukluklarda daha fazla semptom şiddeti, kötü hastalık prognozu ve işlevsellikte bozulma ile ilişkili olduğu gösterilmiştir (28). Benzer şekilde alkol ve madde kullanım bozukluklarında da algılanan sosyal destek düzeyleri, bağımlılığın tedaviye cevabı ve seyri ile doğrudan ilişkili bulunmuştur (9,10,17,29). Ateş ve ark. (5) yaptıkları çalışmada; bağımlılık tedavisinde en önemli hedeflerden birinin yaşam kalitesini arttırmak olduğunu ve alkol/madde kullanım bozukluğu olan hastaların yaşam kalitesi ile algılanan sosyal destek düzeyleri arasında anlamlı bir ilişkinin varlığını bildirmişlerdir. Başka araştırmalarda da; OpKB olan kişilerde akran destek hizmetleri, 12 adımlı tedavi gibi sağlanan sosyal destek düzeylerinin remisyon sürelerine olumlu etkileri olduğu gösterilmiştir (18,30,31). Ancak görüldüğü gibi çalışmamızın sonuçlarıyla bu bulgular çelişmektedir. Analizlerimiz sonucunda; OpKB olan kişilerin algılanan sosyal destek düzeylerinin remisyon kalma süresi ile istatistiksel bir ilişki saptanmamasını iki şekilde yorumlayabiliriz. Birincisi; kronik yineleyici bir hastalık olan opioid bağımlılığında sosyal faktörlere nazaran nörobiyolojik mekanizmaların hastalığın ortaya çıkışı ve relapslardan daha çok sorumlu olduğu, biyolojik tedavilerin remisyon kalma süresine olumlu katkı sağladığına işaret eder (32,33). İkincisi; her ne kadar psikososyal faktörlerin önemli bir ayağı olan güçlü sosyal destekler biyolojik tedavi ile birlikte daha etkin bir sonuca götürmesi olası olsa bile (34) bu bireylerde sık relapsı engelleyen ve uzun süre remisyon kalmalarına katkı sağlayan en az algılanan sosyal destek kadar veya daha önemli belirleyici faktörlerin olması muhtemeldir (4,35). Özellikle uygun ilaçlarla tedavi edilen hastalar; kendi kararlarını alabilme, aile ve topluma katkı sağlama ve bireyin maksimum potansiyeline ulaşabilme becerisini de içeren tam bir iyileşme yolunda ilerler (36,37).

Daha iyimser bir yaklaşımla; bu kişilerin düzenli ilaç kullanmalarını sağlanan sosyal destek olarak değerlendirdiğimizde; OpKB olan kişilerde sağlanan sosyal destek düzeylerinin remisyon kalma süresi ile pozitif ilişkisi olduğu ancak algılanan sosyal destek düzeylerinin remisyon kalma süreleri ile herhangi bir ilişkisi olmadığı speküle edilebilir.

Daha önce Türkiye’de OpKB olan erkek hastalarda yapılmış bir araştırmada algılanan sosyal destek düzeyi düşük olanlarda daha fazla depresif belirtiler ve daha sık relaps tespit edilmiş (19). Bu araştırmanın örneklem sayısı bizim araştırmamıza göre daha

düşük olmakla birlikte algılanan sosyal destek düzeyi ile ilişkili olduğu bulunan faktör relaps sayısıdır. Biz araştırmamızda algılanan sosyal destek düzeylerinin relaps sayısı ile değil remisyon kalma süresi ile ilişkisini değerlendirdik. Ayrıca bu araştırmada örneklem algılanan sosyal destek düzeylerine göre gruplandırılmıştır. Çok boyutlu algılanan sosyal destek ölçeğinin bilinen kesme puanı olmadığı için örneklemin algılanan sosyal destek ölçek puanına göre gruplandırılması bu araştırmanın bulguları ile bizim bulgularımız arasındaki uyumsuzluğu açıklayabilir (19). Bu çalışmanın bulguları tedaviye olumlu yanıt ve remisyon sürelerinin uzunluğu ile daha çok tıbbi tedavi arasındaki ilişkinin önemini ortaya koymaktadır. Tıbbi ve psikiyatrik bir bozukluk olarak bağımlılık tedavisinde ilaç kullanımının daha ön planda olması gereği ile aynı yönde olan çalışma bulgularımız tıpta medikal tedavilerin yadsınamaz önemine vurgu yapar.

Biz çalışmamızda algılanan sosyal destek yanı sıra relapsta kalma süresini uzatması muhtemel faktörleri de gözden geçirdik. Bulgularımızdan biri de; şehirde yaşayan OpKB olanların remisyon sürelerinin kırsalda yaşayanlara göre anlamlı düzeyde yüksek olmasıdır. Bu bulgu; şehirde yaşayanların sağlık hizmetlerine ulaşma imkanlarının daha kolay olması, dolayısıyla ilaç tedavisine daha kolay ulaşabilmeleri ile ilişkilendirilebilir. Eğer kişi sağlık hizmetine kolay ulaşabiliyor ve düzenli ilaç tedavisi ile idamesi sağlanıyorsa remisyon süresinin uzayabileceği öne sürülebilir. Ayrıca şehirde yaşayan bireylerin kırsalda yaşayanlara göre sağlık okur-yazarlık düzeylerinin daha iyi olduğu ve hastalıklarının tedavisinin yönetiminde daha doğru kararlar aldıkları bildirilmiştir (38). Buna göre; şehirde yaşıyor olmak hem sağlık hizmetlerine kolay ulaşma açısından bir avantaj olmakla birlikte bu kişilerin tedavide kalma ve tedavilerini doğru yönetmeleri açısından da bir avantaj gibi görünmektedir.

Çalışmamız sadece opioid kullanan ve başka madde kullanımı olmayan büyük bir hasta grubunda yapılmış olması çalışmamızı güçlü kılmaktadır. Ancak araştırmanın deseninde hasta grupları oluşturulurken remisyon süresine göre 1 yıldan kısa ve 1 yıldan uzun olarak ayrılmış olmasının, bu durumda örneğin 11 aydır remisyon kalma süresinde olan hastalar ve 1 aydır remisyon kalma süresinde olan hastaların aynı grupta değerlendirilmesinin araştırma sonuçlarını etkilemiş olabileceğini düşündük. Bu kısıtlılığın etkisini araştırmak için tüm hastaların remisyon süresini ay olarak hesaplayıp algılanan sosyal destek düzeyleri ile ilişkisine

baktık. Ancak bulgularımız yine OpKB hastalarında algılanan sosyal destek düzeyi ve remisyon süreleri arasında istatistiksel olarak anlamlı bir ilişki olmadığı yönündeydi ( $p=0,363$ ).

Sonuç olarak, OpKB olan kişilerde remisyon süreleri ile ilaç tedavisi alıyor olmanın ilişkili olduğu, şehirde yaşamının ve tıbbi desteğe kolay ulaşabilmenin bu ilişkiye olumlu katkı sağladığı, bunun yanında kişilerin algıladıkları sosyal destek düzeylerinin remisyonunda kalma süresi ile anlamlı bir ilişkisi olmadığı söylenebilir. Bu kişilere sağlanan gerçek sosyal destek düzeylerinin belirlenmesinde kullanılan subjektif ölçekler doğru sonuca ulaşmada yetersiz kalabilmekte, doğru sonuçlara ulaşabilmek için sosyal destek düzeylerinin daha objektif ve çok yönlü değerlendirilmesi gerekmektedir. OpKB olan kişilerde algılanan ve sağlanan sosyal desteğin kişilerin remisyonunda kalma sürelerine ne düzeyde katkıda bulunduğunun belirlenebilmesi ve nedensellik ilişkisinin kurulabilmesi için daha geniş örneklemli, çok yönlü değerlendirmelerin yapıldığı izlem çalışmalarına ihtiyaç vardır.

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# Inter Observer Agreement of The Modified Ishak Histological Activity Index in Chronic Viral Hepatitis Among Pathologists Trained in Different Centers

## *Kronik Viral Hepatitlerde Modifiye Ishak Histolojik Aktivite İndeksinin Farklı Merkezlerde Eğitim Almış Patologlar Arasında Tekrarlanabilirliği*

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### Öz

**Amaç:** Karaciğer biyopsisi kronik hepatitli hastalarda hepatic hasarın gösterilmesinde altın standarttır. Bu çalışmada, kronik hepatitlerin histopatolojik değerlendirmesinde kullanılan Modifiye Ishak Histolojik Aktivite İndeksi (MHAİ)'nin farklı merkezlerde eğitim almış gözlemciler arası tekrarlanabilirliği araştırılmıştır.

**Hastalar ve Yöntem:** Çalışmaya 2020-2023 yılları arasında toplam 64 karaciğer iğne biyopsisi dahil edildi. Olgulara ait hematoksin-eozin, gümüş ve trikrom ile boyanmış kesitler araştırmacı (İÇ) tarafından ışık mikroskopunda tekrar değerlendirildi ve MHAİ'ne göre tekrar skorlandı. İstatistiksel değerlendirmede SPSS 21.0 programı kullanılarak Cohen'in kappa istatistiği uygulandı.

**Bulgular:** İstatistiksel değerlendirmede tüm olgular dikkate alındığında kappa değeri; MAİ derece için 0.02(slight), evre için 0.38(fair) bulundu. Araştırmacının diğer patologlar ile uyumu değerlendirildiğinde derecelendirmede kappa değerleri oldukça düşük olup uyumsuz bulundu. Evrede ise dereceye göre daha yüksek değerler( 0.12-0.49) olmakla birlikte uyum zayıf ve orta derece idi. Ancak uzun vadeli işbirliği geçmişine sahip patologlar, devam eden bilgi alışverişinin önemini vurgulayarak daha yüksek düzeyde uyum gösterdiler.

**Sonuç:** Bu çalışma, MHAİ puanlamasının tekrarlanabilirliğini artırmak için yorumlanması ve uygulanmasını yönelik standart bir yaklaşıma duyulan ihtiyacı vurgulamaktadır.

**Anahtar Kelimeler:** Kronik hepatit, gözlemciler arası uyum, Modifiye Ishak Aktivite İndeksi

### Abstract

**Aim:** Liver biopsy is the gold standard for demonstrating hepatic damage in patients with chronic hepatitis. In this study, the reproducibility of the Modified Ishak Histological Activity Index (MHAİ), used in the histopathological evaluation of chronic hepatitis, between observers trained in different centers was investigated.

**Patients and Methods:** A total of 64 liver needle biopsies were included in the study between 2020 and 2023. Sections of the cases stained with hematoxylin-eosin, silver and trichrome were re-evaluated under a light microscope by the investigator (İÇ) and re-scored according to MHAİ. In statistical evaluation, Cohen's kappa statistics were applied using the SPSS 21.0 program.

**Results:** When all cases are taken into consideration in statistical evaluation, kappa value is; MAİ was found to be 0.02 (slight) for degree and 0.38 (fair) for stage. When the researcher's compatibility with other pathologists was evaluated, the kappa values in the grading were quite low and found to be incompatible. Although there were higher values (0.12-0.49) in the stage than in the degree, the fit was poor and moderate. However, pathologists with a long-term history of collaboration showed higher levels of compliance, highlighting the importance of ongoing exchange of information.

**Conclusion:** This study highlights the need for a standardized approach to interpretation and application of MHAİ scoring to increase reproducibility.

**Keywords:** Chronic hepatitis, interobserver agreement, Modified Ishak Activity Index

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**INTRODUCTION**

Liver biopsy is considered the gold standard for demonstrating hepatic damage in patients with chronic hepatitis. It not only determines the severity of hepatitis during the biopsy but also enables the assessment of treatment effectiveness. Treatment decisions are heavily reliant on both laboratory findings and the biopsy result, which, in turn, dictates the severity of the liver disease. Detecting fibrosis at an early stage can be pivotal in preventing the disease from progressing. Consequently, it is crucial that the reports resulting from the pathological examination of needle biopsies are not only reliable but also repeatable. However, the nature of pathological examination is inherently subjective.

To address this subjectivity and to establish a common language among pathologists for the sake of clinical relevance, various grading and scoring systems have been developed for many diseases. These systems aim to quantify the severity and extent of the disease, thereby providing insights

into its course. The initial histological classification of hepatitis dates back to 1968 when De Grote and colleagues introduced it (1). The Histological Activity Index (HAI), proposed by Knodell et al. in 1982, marks the inception of scoring systems for chronic hepatitis (2). The modified Knodell HAI score, as refined by Ishak et al., stands as the most widely employed method in contemporary practice (3). Furthermore, the Scheuer and Metavir systems are routinely adopted by numerous pathologists (4,5). All these methods seek to quantify necroinflammatory activity and fibrosis prevalence in the liver through numerical scores. However, the inherent challenge lies in the fact that these grading and scoring systems rely heavily on subjective descriptions. Pathologists are tasked with interpreting findings, classifying them, and assigning numerical values based on these verbal expressions, which can often lead to discrepancies among pathologists' assessments.

Ideally, a scoring system should confidently serve the purposes of treatment planning and treatment

**Table 1.** Modified Histological Activity Index Grading

•A Piecemeal necrosis	•None	0
	•Mild (focal, few portal areas)	1
	•Mild/Moderate (focal, most portal areas)	2
	•Moderate (less than 50% continuous tracts or septa)	3
	•Severe (more than 50% continuous in tracts or septa)	4
•B Confluent necrosis	•None	0
	•Focal confluent necrosis	1
	•Zon 3 necrosis in some areas	2
	•Zon 3 necrosis in most areas	3
	•Zon 3 necrosis + occasional portal-central (P-C) bridging	4
	•Zon 3 necrosis + multiple portal-central (P-C) bridging	5
•C Focal necrosis/inflammation	•Panacinar or multiacinar necrosis	6
	•1 or fewer foci (per x10 magnification)	1
	•2-4 foci (per x10 magnification)	2
	•5-10 foci (per x10 magnification)	3
•D Portal inflammation	•More than 10 foci (per x10 magnification)	4
	•None	0
	•Mild (some or all portal areas)	1
	•Moderate (some or all portal areas)	2
	•Moderate/Marked (all portal areas)	3
	•Marked (all portal areas)	4

**Table 2.** Modified Histological Activity Index Staging

• No fibrosis	0
• Fibrous expansion of some portal areas and +/- short fibrous septa	1
• Fibrous expansion of most portal areas and +/- short fibrous septa	2
• Fibrous expansion of most portal areas with occasional portal-portal (P-P) bridging	3
• Fibrous expansion of most portal areas with marked P-P bridging as well as portal-central (P-C) bridging	4
• Marked bridging (P-P and/or P-C) with occasional nodules (incomplete cirrhosis)	5
• Cirrhosis (possible or definite)	6

**Table 3.** Kappa values between researchers and other pathologists in the MHAİ assessment (n=64).

	MHAİ grade	MHAİ stage	A Piecemeal necrosis	B Confluent necrosis inflammation	C Focal necrosis/ inflammation	D Portal
KAPPA	0.02	0.38	0.29	-0.31	0.31	0.41

**Table 4.** Kappa values between researchers and other pathologists in the MHAİ assessment (n=10).

Kappa	P1(n=10)	P2(n=10)	P3(n=10)	P4(n=10)	P5(n=10)	P6(n=10)
MHAİ grade	-0.08	0.02	-0.01	0.10	0	0.07
MHAİ grade by diagnostic categories *	0	0.40	0.34	0.58	0.20	0.38
MHAİ stage	0.12	0.25	0.49	0.72	0.23	0.32
A Piecemeal necrosis	0.11	0.39	0.48	0.17	0.31	0.23
B Confluent necrosis	0	-0.15	0.20	0.10	0.03	0.05
C Focal necrosis/ inflammation	0.26	0.40	0.14	0.52	0.26	-0.29
D Portal inflammation	0.50	0.34	0.59	0.16	0.31	0.53

\*(Score 1-3; minimal hepatitis, score4-8; mild hepatitis, score9-12; moderate hepatitis, score13-18; severe hepatitis)

effectiveness assessment, while simultaneously exhibiting high interobserver repeatability. This study, therefore, endeavors to explore the interobserver repeatability of the widely used Modified Ishak Histological Activity Index (MHAİ) in the histopathological evaluation of chronic hepatitis. Observers trained at different centers are the subjects of this investigation.

**PATIENTS AND METHODS**

This study is approved by the Local Ethics Committee (Approval number: 4/2023). Between 2020 and 2023, a total of 64 needle liver biopsies were included in this study. Biopsy reports were retrieved from the electronic archive. These biopsies had been reported by seven pathologists working in our department who received specialized training from different centers. Ten reports from each of six pathologists were included in the study. The seventh pathologist, who had recently joined the study, had only four biopsies meeting the criteria and was not evaluated individually. All biopsies had received a diagnosis of chronic hepatitis and were scored according to the Modified Ishak Histological Activity Index (MHAİ) (Table 1).

Sections stained with hematoxylin-eosin, silver, and trichrome were retrieved from the archives and re-evaluated by the researcher (İÇ) under a light microscope. They were then rescored according to the MHAİ. The data were compared with the values from the previously prepared reports. In the initial evaluation, the researcher scores were compared to all other biopsies (n=64) (Table 2). Subsequently, the scores from the researcher and those from the six pathologists were compared individually (n=10) (Table 3).

Statistical analysis was performed using SPSS 21.0, applying Cohen's kappa statistic. The results were evaluated by categorizing them into standard categories as follows (6).

Cohen's Kappa	Interpretation
<0	poor
00-0.20	slight
0.21-0.40	fair
0.41-0.60	moderate
0.61-0.80	substantial
0.81- 1.00	almost perfect

## RESULTS

In the statistical evaluation, considering all cases, the kappa value for the MAI degree was 0.02 (slight), and for the stage, it was 0.38 (fair). When considering individual parameters, the lowest kappa value was found for B (confluent necrosis), while the highest kappa value was observed in the D (portal inflammation) category (Table 3).

When evaluating the researcher's agreement with other pathologists separately, the kappa values for grading were quite low, indicating poor agreement. For staging, there were relatively higher values (ranging from 0.12 to 0.49), indicating fair to moderate agreement. Substantial agreement (0.72) was observed with one observer (P4). Among the parameters, the highest agreement was found in the assessment of portal inflammation (D), while the weakest agreement was observed in the assessment of confluent necrosis.

The MHAİ grading was also evaluated as diagnostic categories. In this case (score 1-3 minimal hepatitis, score 4-8 mild hepatitis, score 9-12 moderate hepatitis, score 13-18 severe hepatitis), the kappa values were higher but still did not surpass the weak agreement category (Table 4).

## DISCUSSION

Studies in the literature investigating the reproducibility and interobserver concordance of scoring methodologies have often reported moderate to low levels of agreement (7–10). This phenomenon can be primarily attributed to variations in individual interpretation when translating verbal descriptions into numerical values in semi-quantitative scoring systems. In our study, we did not observe a high level of agreement among the data assessed by the primary researcher and the other pathologists working within the same institution. The highest level of agreement was achieved with a pathologist (P4) who had a long history of collaboration. This suggests that ongoing consultations and knowledge exchange over the years may have contributed to a shared understanding among these individuals. In a study involving pathologists from the same institution, interobserver agreement in the modified HAI scoring system reportedly reached 95-96% (11). However, in institutions like ours, where pathologists have received training from different institutions and represent diverse schools of thought, interobserver agreement tends to be low, aligning with the findings of certain studies in the literature (7,9,10).

Due to the limited repeatability associated with semi-quantitative scoring systems, there has been a growing interest in the application of computer-assisted morphometry based on image analysis as an alternative approach. In recent years, numerous studies have employed computer-assisted automated algorithms for quantifying fibrosis using biopsy images (12–14). These investigations have convincingly demonstrated that automated fibrosis measurements exhibit greater precision in detecting variations in hepatic fibrosis compared to semi-quantitative histological staging (13,15). Nevertheless, it is imperative to acknowledge that these methods are not without their challenges. Assessing fibrosis in hepatitis necessitates evaluating structural alterations, nodular formations, and changes in microcirculation, in addition to quantifying the increase in fibrous tissue. The automatically measured quantity of fibrous tissue may fail to capture the architectural pattern of fibrosis distribution. Hence, it might be more suitable to combine automatic image analysis with semi-quantitative scoring for histological staging in cases of chronic hepatitis (16).

## CONCLUSION

The Knodell HAI method has been a milestone in liver pathology due to its pioneering role in enabling the comparison of pathology reports for the same sample by different pathologists (17). Although modifications have been made by Ishak, even among globally recognized experts in the field, there are issues with repeatability. Given its direct impact on patient management, there is an evident need for more objective approaches. This underscores the necessity to establish consensus among observers regarding what is meant by the semi-quantitative descriptions and expressions used in the parameters and to create a common approach for implementing scoring.

Furthermore, it is advisable to replace vague expressions such as several or many with more objective numerical values in the descriptions used in scoring systems. Additionally, supplementing the HAI scoring system with schematic images based on it could enhance repeatability, similar to the approach taken in Gleason scoring (18).

Moreover, the use of standardized histometric measurements alongside scoring systems for the assessment of necroinflammation and fibrosis is believed to improve concordance. Further studies on this topic will shed more light on this subject.

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# Hematological Involvement in Sjögren's Syndrome and The Relationship of Involvement with Salivary Gland Biopsy

## Sjögren Sendromunda Hematolojik Tutulum ve Tutulumun Tükrük Bezi Biyopsisi ile İlişkisi

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### Öz

**Amaç:** Sjögren sendromu (SS), glandular bez iltihabı ile karakterize kronik, multisistemik otoimmün hastalıktır. SS hematolojik tutulum da dahil çok farklı ekstraselüler tutulumlar yapabilmektedir. Çalışmamızın amacı SS hastalarında hematolojik ve patolojik veri olan Fokus skoru (FS) ve Mason Chisholm Skoru (MS) ile ilişkisini değerlendirmektir.

**Hastalar ve Yöntemler:** Çalışmaya 101 SS olan hasta ve 91 kontrol grubu alınmıştır. Tüm SS hastalarına 2016ACR/EULAR kriterlerine göre yeni tanı konmuştur. Hemogram bozukluğuna neden olabilecek ek hastalıklara sahip hastalar çalışmadan dışlanmıştır.

**Bulgular:** Nötrofil, monosit ve platelet değerleri istatistiksel olarak anlamlı düşük çıkmış ( $p=0.000$ ,  $p=0.002$ ,  $p=0.016$ ); lenfosit ve hemoglobin değerleri kontrol grubuna göre düşük olsa da istatistiksel olarak anlamlı çıkmamıştır ( $p=0.053$ ,  $p=0.685$ ). Korelasyon analizinde hem FS ve MS'unun nötrofil ( $r=-0.329$ ,  $p<0.01$ ), lenfosit ( $r=-0.264$ ,  $p<0.01$ ), monosit ( $r=-0.306$ ,  $p<0.01$ ) ve platelet ( $r=-0.220$ ,  $p<0.01$ ) ile negatif korele bulunmuştur.

**Sonuç:** SS hemogramda sitopeniler yapabilmektedir ve nötropeni, anemi ve trombositopeni, FS ve MS ile negatif korelasyon göstermektedir. Bu yüzden tanı anında yüksek FS ve MS olan hastalarda hematolojik tutulum açısından dikkatli olunmalı, hastalar SS kriterlerini karşılarsa dahi minör tükrük bezi biyopsisi yapılmalıdır.

**Anahtar Kelimeler:** Sjögren sendromu, minör tükrük bezi biyopsisi, fokus skoru, sitopeni

### Abstract

**Aim:** Sjögren's syndrome (SS) is a chronic, multisystem autoimmune disease characterized by inflammation of the glandular tissues. SS can manifest with various extraglandular involvements, including hematologic complications. The aim of our study is to evaluate the relationship between hematologic and pathological data, specifically focusing on the Focus Score (FS) and the Mason Chisholm Score (MS), in SS patients.

**Patients and Methods:** The study included 101 patients with Sjögren's syndrome (SS) and 91 individuals in the control group. All SS patients were newly diagnosed according to the 2016 ACR/EULAR criteria. Patients with comorbidities that could lead to hematological disorders were excluded from the study.

**Results:** The neutrophil, monocyte, and platelet values were found to be statistically significantly lower ( $p=0.000$ ,  $p=0.002$ ,  $p=0.016$ ), while lymphocyte and hemoglobin values, although lower in the SS group compared to the control group, did not reach statistical significance ( $p=0.053$ ,  $p=0.685$ ). Correlation analysis revealed a negative correlation between both the FS and MS scores and neutrophil ( $r=-0.329$ ,  $p<0.01$ ), lymphocyte ( $r=-0.264$ ,  $p<0.01$ ), monocyte ( $r=-0.306$ ,  $p<0.01$ ), and platelet ( $r=-0.220$ ,  $p<0.01$ ) values.

**Conclusion:** SS can potentially induce cytopenias in the hemogram, with neutropenia, anemia, and thrombocytopenia displaying a negative correlation with FS and MS. Consequently, in patients with elevated FS and MS scores at the time of diagnosis, it is crucial to exercise caution regarding hematological involvement. Even if patients meet the SS diagnostic criteria, a minor salivary gland biopsy should be considered.

**Keywords:** Sjögren syndrome, minor salivary gland biopsy, focus score, cytopenia

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## INTRODUCTION

Sjögren syndrome (SS) is a chronic, multisystem autoimmune disease characterized by inflammation of the tear and salivary glands, resulting in dryness of the eyes and mouth. It can also manifest with various extraglandular symptoms. This pathology, described by some authors as autoimmune epithelitis, can occur independently or coexist with other autoimmune diseases (1).

Between 60 to 80 percent of individuals affected by Sjögren's syndrome are characterized by the presence of autoantibodies, particularly anti-Ro/SSA and anti-La/SSB. Antinuclear antibodies (ANA) are found in approximately 90 percent of patients, and high titers of rheumatoid factor are also frequently observed. Autoantibodies can be positive years before the clinical onset of SS (2). The primary pathological lesion of Sjögren's syndrome is lymphocytic infiltration of the salivary and lacrimal glands. The infiltrates consist of focal clusters of lymphocytes that start around the ducts and extend to involve the entire lobule. The cellular composition of these infiltrations depends on the severity of the disease. Initially, T cells, especially CD4+ cells, dominate in milder infiltrates that conform to the gland's architecture. B cells become more prominent in larger and denser infiltrates associated with acinar destruction and loss of tissue structure (3).

Patients with SS have an increased risk of non-Hodgkin lymphoma compared to the general population. This association is well-established for various autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, and celiac disease, but the highest risk is observed in SS patients (4). Persistent enlargement of the salivary glands is a significant clinical risk factor. Other risk factors include cutaneous vasculitis, lymphadenopathy, splenomegaly, cryoglobulinemia, and the development of glomerulonephritis (5). SS can also lead to anemia and leukopenia, especially in patients positive for SS-A and SS-B antibodies (6).

The purpose of our study is to examine the cellular types of hematological involvement in SS patients and evaluate the relationship between cellular involvement and pathological data using the Focus Score (FS) and Mason Chisholm Score (MS).

## PATIENTS AND METHODS

### *Study population*

The study included a total of 101 patients diagnosed with primary Sjögren's syndrome who visited

the Rheumatology outpatient clinic at Necmettin Erbakan University Medical Faculty Hospital between 01.03.2021 and 01.12.2021. The study was approved by the medical ethics committee of the hospital (07.04.2023- 2023/4279/13662). A control group of 91 individuals who underwent salivary gland biopsy for various reasons was also included. All participants included in this study were newly diagnosed with SS and had not received any prior treatment for SS. Minor salivary gland biopsy samples were collected from the patients and evaluated by two experienced pathologists.

Patients with concomitant autoimmune diseases, lymphoproliferative diseases, malignancies, end-stage renal and liver disease, diabetic nephropathy, active infections, recent blood transfusions, and a previous history of anemia, were excluded from the study.

### **Demographic and clinical data**

All patients underwent Schirmer's test and ANA test. In patients with positive ANA results, ENA (extractable nuclear antibody) analysis was performed. Minor salivary gland biopsy was performed on all patients. ANA was evaluated using the indirect immunofluorescence (IIF) method, and ENA profile was assessed using the Immun Blot (IB) method. The values of Schirmer's test, ANA, ENA profile (including SS-A, SS-B, RO-52), and pathological data were recorded for each patient. The diagnosis of Sjögren's syndrome was established according to the 2016 ACR/EULAR criteria.

### **Statistical analysis**

Data analysis was conducted using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant. The normality of variables was assessed using the Kolmogorov-Smirnov test, and it was found that all continuous variables had a non-normal distribution. Continuous variables were presented as mean (standard deviation), while categorical variables were presented as numbers and percentages. The comparison of findings between the two groups was performed using the Chi-square test and Mann-Whitney U test. Correlations were analyzed using the two-tailed Spearman correlation analysis.

## RESULTS

A total of 101 patients with primary Sjögren's syndrome and 91 individuals in the control group were included in the study. The demographic and serological information of patients diagnosed with

**Table 1.** Demographic Data in Primary Sjögren's Syndrome

Variables	Values
Age (year old)	51.1 (±12.9)
Female gender (N, (%))	95 (94.0%)
ANA (N)	
Negative	17 (16.9%)
Positive	84 (83.1%)
ENA (N)	
Negative	40 (39.6%)
SS-A	20 (19.8%)
SS-B	2 (1.9%)
RO-52	30 (29.7%)
Multiple Positive	9 (8.9%)
Schirmer Score	3.63 (±3.1)

Note: Values are expressed as mean (± SD), Number(N) and percentage(%)

SS is displayed in Table 1. No statistically significant variations in age and gender distribution were observed between the patient group and the control group. As anticipated, the Focus Score and Mason Chisholm scoring systems, which are acknowledged as pathological classifications for SS, demonstrated statistically significant differences in the patient group compared to the control group.

When examining the hemogram results of the patients, it was observed that there was a decrease in both the myeloid and lymphoid series cells. Among them, neutrophil, monocyte, and platelet values were found to be statistically significantly lower ( $p=0.000$ ,  $p=0.002$ ,  $p=0.016$ ); although lymphocyte and hemoglobin values were lower in the patient group compared to the control group, they did not

**Table 2.** Comparison of pathology and hemogram results of patients with primary Sjögren's syndrome

Variables	SS	Control	P
Sex (Female) N(%)	95 (94.0%)	79 (86.8%)	0.135 <sup>1</sup>
Age (years)	51.5(±12.9)	46.6(±13.1)	0.104 <sup>2</sup>
Focus Score			<0,001 <sup>2</sup>
<1	6 (5.9%)	91 (100%)	
=1	74 (73.2%)		
>1	21 (20.7%)		
Mason Chisholm Score	3.48 (±0.74)	1.37(±0.69)	<0.001
0	0 (0%)	17 (18.7%)	
1	4 (3.9%)	38 (41.8%)	
2	2(1.9%)	35 (38.5%)	
3	37 (36.6%)	1 (1.1%)	
4	58 (57.4%)	0 (0%)	
WBC	6.53(±2.3)	8.01(±2.6)	0.637 <sup>2</sup>
NEU	3.82(±1.8)	4.86(±2.3)	0.000 <sup>2</sup>
LYM	2.12(±0.8)	2.4(±0.8)	0.053 <sup>2</sup>
MON	0.48 (±0.17)	0.54 (±0.15)	0.002 <sup>2</sup>
HGB	13.1 (±1.2)	13.2 (±1.3)	0.685 <sup>2</sup>
PLT	292(±326)	289(±83)	0.016 <sup>2</sup>

<sup>1</sup> Fisher's Exact Test, <sup>2</sup> Mann-Whitney U test

Note: Results are provided as mean ± SD for continuous variables and number (percentage) of patients for categorical variables. Abbreviations: WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; MON monocytes; HGB, hemoglobin; PLT, platelet

**Table 3.** Correlation of Hemogram and Pathological Scoring Grades

	1	2	3	4	5	6	7
1 WBC	1						
2 NEU	0.912*	1					
3 LYM	0.608*	0.329*	1				
4 MON	0.534*	0.451*	0.369*	1			
5 HGB	-0.017	-0.053	0.102	-0.041	1		
6 PLT	0.422*	0.390*	0.296*	0.272*	-0.137	1	
7 Focus Score	-0.106	-0.301*	-0.240*	-0.229*	-0.056	-0.204*	1
8 Mason Score	-0.139	-0.329*	-0.264*	-0.306*	-0.113	-0.220*	0.887*

WBC, white blood cell; NEU, neutrophil; LYM, lymphocyte; MON monocytes; HGB, hemoglobin; PLT, platelet \* $p<0.01$

reach statistical significance ( $p=0.053$ ,  $p=0.685$ ). The comparison of pathology and hemogram results in SS patients is presented in Table 2.

The correlation analysis between hemogram values and FS and MS is presented in Table 3. In the correlation analysis between FS and hemogram values, a negative correlation was found with neutrophil ( $r=-0.301$ ,  $p<0.01$ ), lymphocyte ( $r=-0.240$ ,  $p<0.01$ ), monocyte ( $r=-0.229$ ,  $p<0.01$ ), and platelet ( $r=-0.204$ ,  $p<0.01$ ) values. Similarly, in the MS score, a negative correlation was observed with neutrophil ( $r=-0.329$ ,  $p<0.01$ ), lymphocyte ( $r=-0.264$ ,  $p<0.01$ ), monocyte ( $r=-0.306$ ,  $p<0.01$ ), and platelet ( $r=-0.220$ ,  $p<0.01$ ) values. Additionally, as expected, a positive correlation was found between FS and MS ( $r=-0.887$ ,  $p<0.01$ ).

## DISCUSSION

In our study, it was observed that both monocytes and lymphocyte series cells showed a decreasing trend in the hemogram results of the patients. Among them, neutrophil, monocyte, and platelet values were found to be statistically significantly lower, while lymphocyte and hemoglobin values were lower in the patient group compared to the control group, but did not reach statistical significance. In the correlation analysis, it was found that both FS and MS were negatively correlated with neutrophil, lymphocyte, monocyte, and platelet values.

Leukopenia has been reported in both case studies and large-scale epidemiological investigations (7-9). Furthermore, a few studies have suggested that it may be a risk factor for lymphoma (10-12). However, the clinical characteristics and underlying pathogenic mechanisms of leukopenia associated with SS have not been completely clarified. In our study, similar to the literature, we observed a decreased white blood cell count in SS patients compared to the control group, but it did not reach statistical significance.

There are no studies specifically focusing on SS and neutropenia in the literature. Most studies in this area are generally related to the etiopathogenesis of neutropenia in SLE. One study conducted on SLE patients with neutropenia showed a significant negative correlation between neutrophil count and serum Tumor Necrosis Factor-Related Apoptosis Inducing Ligand (TNFSF10/TRAIL) levels (13). TRAIL has been reported to be associated with the pathogenesis of some autoimmune diseases such as Sjögren's syndrome, autoimmune encephalomyelitis, and thyroid disease (14-16). The exact pathogenesis

of neutropenia in SS is not fully understood. In our study, we also observed a statistically significant decrease in neutrophil levels in SS patients compared to the control group. The decrease in neutrophil levels showed a negative correlation with FS and MC in the minor salivary gland biopsy.

Autoimmune diseases are frequently complicated by immune thrombocytopenic purpura (ITP), although the precise mechanisms underlying platelet destruction remain uncertain (17). Elevated levels of plasma P-selectin autoantibodies have been proposed to potentially contribute to the pathogenesis of ITP in patients with SS (18). Chen et al. (19) highlighted a significant decrease in FcγRIIb expression on B cells in SS patients with severe thrombocytopenia. These studies suggest the involvement of humoral immune response in platelet destruction in SS. However, the specific autoantibodies that may contribute to platelet destruction and the involvement of T cells in ITP in SS have not been investigated yet. Consistent with the literature, our study also revealed statistically significant thrombocytopenia in SS patients compared to the control group. Furthermore, thrombocytopenia showed a negative correlation with the Focus score and Mason Chisholm score.

Mild normocytic normochromic anemia is frequently observed in patients with SS (20). Severe anemia is uncommon, and in the literature, only a few cases of severe autoimmune hemolytic anemia (AIHA) have been reported (21). Tishler et al. (22) noted that elderly-onset SS patients tend to have slightly milder clinical symptoms and fewer immunological markers compared to younger-onset SS patients. Studies have shown that AIHA in SS patients is associated with a higher prevalence of autoantibodies (ANA, SSA, etc.) compared to those without anemia, and the anemia tends to be more severe (23). Consistent with the literature, our study observed a decrease in hemoglobin levels in SS patients compared to the control group, although it was not statistically significant.

In a study investigating lymphocytes, it was observed that naïve CD4+ T cells in SS patients had a lower frequency of Ki67+ cell proliferation compared to the control group. Additionally, naïve CD4+ T cells obtained from SS patients showed decreased proliferative response to in vitro IL-7 stimulation, suggesting impaired homeostatic T-cell proliferation in individuals with the disease (24). In our study, lymphocyte count in SS patients showed a decrease similar to the literature but was not statistically

significant compared to the control group. However, a negative correlation was observed between FS and MS scores based on the salivary gland biopsy results.

Numerous studies in the literature have demonstrated the association between monocytes and the pathogenesis of SS. TRAIL is a cytokine that plays a role in the regulation of immunity. Studies have shown that TRAIL plays a critical role in SLE, other rheumatic diseases, and lung damage (25-28). In a study, researchers demonstrated an elevated expression of TRAIL in monocytes of SS patients, suggesting that TRAIL-expressing monocytes may have a significant role in the pathogenesis of SS (29). Wildenberg et al. (30) also reported an increase in IFN-associated genes, such as IFI27, IFITM1, IFIT4, and IFI44, in monocytes of SS patients. Despite the studies mentioned concerning the association between monocytes and SS pathogenesis, no study related to monocyte depletion has been found. In our study, we observed a decreased level of monocytes in SS patients compared to the control group. Furthermore, the monocyte count showed a negative correlation with the focus score and MS score.

In our study, we observed a decrease in all hematological series, and statistically significant lower levels of neutrophils, monocytes, and platelets were found. The negative correlation between the levels of neutrophils, lymphocytes, monocytes, platelets, and the FS and MS was interpreted based on the results of minor salivary gland biopsy. Although there was a decrease in leukocyte and lymphocyte levels, the results did not reach statistical significance, which could be attributed to the early stage of the disease at the time of diagnosis. Our study found that hematological involvement increased with the histopathological grade of minor salivary gland involvement after biopsy. Upon reviewing existing studies, it was found that only lymphocyte and leukocyte levels were examined in relation to the severity of minor salivary gland involvement. Our study is novel in comparing all hematological cell series with FS and MS.

Neutropenia in patients with Sjögren's syndrome, especially when it drops below 500/ $\mu$ L, may be associated with an increased risk of infection. Autoimmune neutropenias are often undetected since symptoms are not pronounced, and reliable markers for neutrophil lysis are lacking. Bacterial infections, particularly recurrent stomatitis, periodontal inflammation, perirectal abscess, cellulitis, pneumonia, and septicemia, are more common. Considering the decreased exocrine secretions in

SS patients, it can be anticipated that oral cavity, upper and lower respiratory tract infections would be frequent. Although anemia is common in SS patients, AIHA is rare but can lead to severe clinical outcomes. Anemia-related symptoms such as fatigue, weakness, and impaired quality of life may occur. Mild petechiae due to thrombocytopenia, especially in the context of middle-aged to older patient population and multiple medication use, may be associated with gastrointestinal bleeding. In our study, although the patients' initial hemogram results were taken at the time of diagnosis, cytopenias were present compared to the control group, and these cytopenias correlated with salivary gland involvement. Therefore, clinicians should be cautious in patients with high FS and MS, as hematological involvement may increase as the histopathological grade increases. The 2016 ACR/EULAR criteria are commonly used in the diagnosis of Sjögren's syndrome. In classification using scoring, patients can receive a diagnosis without undergoing minor salivary gland biopsy. However, considering that our study showed an increase in hematological involvement as FS and MS increased, it is important to assess hematological involvement despite meeting the diagnostic criteria.

The main limitation of the study is the lack of long-term follow-up of hematological parameters in patients. However, considering that the parameters can be influenced by the treatment administered after diagnosis, a long-term follow-up study was not conducted. The strength of our study is that it was conducted using laboratory values obtained before the initiation of immunosuppressive treatment, which could affect the hemogram results in patients.

## CONCLUSION

SS can cause cytopenias in the hemogram, and there is a negative correlation between neutropenia, anemia, and thrombocytopenia with the FS and MS observed in the salivary gland biopsy. Therefore, in patients with high-grade involvement at the time of diagnosis, caution should be exercised regarding hematological involvement, and even if patients meet the classification criteria for diagnosis, a minor salivary gland biopsy should be performed.

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# The Relationship Between Neutrophil Elastase, IL-1 $\beta$ , IL-8 and Desmosin Levels in Sputum and Blood with Sputum Culture Results in Bronchiectasia Patients

## Bronşektazili Hastalarda Balgam ve Kandaki Nötrofil Elastaz, IL-1 $\beta$ , IL-8 ve Desmosin Düzeylerinin Balgam Kültürü Sonuçları İle İlişkisi

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### Öz

**Amaç:** Çalışmamızda, bu hastalarda kan ve balgamda NE, kanda IL-8, IL-1 $\beta$  ve desmosin düzeylerinin tanısal değerini ve semptomlarla, alevlenme sıklığıyla, etiyolojileriyle, radyolojik tutulum yaygınlığıyla, bronşektazi tipleriyle ilişkilerini araştırmayı amaçladık.

**Hastalar ve Yöntem:** Çalışmaya Kasım 2020-Mart 2021 tarihleri arasında Göğüs hastalıkları polikliniğine başvuran ve kliniğimizde takipli 18-90 yaş arası 46 bronşektazili hasta ve 45 kişilik kontrol grubu alındı.

**Bulgular:** Kanda NE, IL-1 $\beta$ , desmosin hasta grubunda istatistiksel olarak anlamlı derecede yükseldi ( $p<0,001$ ). Biyobelirteçlerin tanısal değeri için ROC analizi yapıldı. Kan NE için kesme değeri 12,70 ng/mL olduğunda duyarlılık %71,7, özgüllük %77,8, IL 1 $\beta$  için kesme değeri 2,935 pg/mL, duyarlılık %73,9, özgüllük ise %73,9 olarak belirlendi. %71,1, desmosin için eşik değeri 0,505 ng/mL, duyarlılığı %67,4 ve özgüllüğü %62,2 idi.

**Sonuç:** Çalışmamızda bronşektazili hastalarda kanda NE, IL-1 $\beta$  ve desmosinin ve balgamda NE'nin önemli inflamatuvar belirteçler olduğu, önemli tanısal değere sahip olduğu ve takip parametrelerinin önemli bir bileşeni olabileceği belirlendi. bu parametreler alevlenmelerin sıklığı ile önemli ölçüde ilişkilidir.

**Anahtar Kelimeler:** Bronşektazi, nötrofil elastaz, desmosin, IL-8, IL-1 $\beta$ , balgam kültürü

### Abstract

**Aim:** In our study, we aimed to investigate the diagnostic value of NE in blood and sputum, blood IL-8, IL-1 $\beta$  and desmosine levels and their relationship with symptoms, frequency of exacerbation, etiology, prevalence of radiological involvement, types of bronchiectasis, as well as sputum cell counts and cultures.

**Patients and Methods:** The study included 46 patients with bronchiectasis aged between 18-90 years, who applied to the Chest Diseases Polyclinic between November 2020 and March 2021 and were followed up by our clinic, and a control group of 45 people.

**Results:** At blood, NE, IL-1 $\beta$ , desmosine were statistically significantly higher in the patient group ( $p<0,001$ ). ROC analysis was performed for the diagnostic value of biomarkers. When the cut-off value for blood NE was 12.70 ng/mL, the sensitivity was 71.7%, the specificity was 77.8%, for IL 1 $\beta$  the cut-off value was 2.935 pg/mL, the sensitivity was 73.9%, the specificity was 71.1%, for desmosine, the cut-off value was 0.505 ng/mL, the sensitivity was 67.4% and the specificity was 62.2%.

**Conclusion:** In our study, it was found that NE, IL-1 $\beta$  and desmosine in blood and NE in sputum in patients with bronchiectasis are important inflammatory markers, have significant diagnostic value, and may be an important component of follow-up parameters, since these parameters are significantly correlated with the frequency of exacerbations.

**Keywords:** Bronchiectasis, neutrophil elastase, desmosine, IL-8, IL-1 $\beta$ , sputum culture

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## INTRODUCTION

Bronchiectasis is a disease characterized by persistent bronchial dilatation associated with chronic neutrophilic airway inflammation (1). It usually presents with symptoms such as cough, sputum production, hemoptysis, recurrent lung infections, weakness and weight loss. In terms of pathophysiology, bronchial dilation leads to impaired mucociliary clearance. Failure to adequately clear bacteria and mucus from the airways causes permanent infection, inflammation, and airway damage. Progressive airway damage can lead to lung dysfunction, worsening of symptoms, and eventually respiratory failure and death. Bronchiectasis may be the last common pathway of severe infections, inflammatory, allergic, genetic and degenerative disorder. Thus, it is the result of multiple pathophysiological processes and one of the most complex and heterogeneous syndromes in respiratory medicine (2). Airway infection as well as exacerbations are critical events in bronchiectasis as they are associated with a marked reduction in quality of life and contribute to disease progression (3). Therefore, the majority of bronchiectasis treatment recommended by the European Respiratory Society (ERS) guidelines is aimed at suppressing airway infection or reducing the frequency of exacerbations (4,5). Biomarkers that can identify patients at risk of exacerbation or active airway infections in real time will help identify patients who need intensive treatment (6). There are limited number of studies on this subject.

Neutrophil elastase (NE), a serine protease produced by neutrophils and released in response to infectious stimuli, has been found to increase in amount during exacerbations of airway disease and decrease with treatment of the exacerbation and resolution of symptoms (7). Desmosin, a biomarker released during NE-related elastin degradation, also shows similar correlations (8). Tsang et al. showed a correlation between sputum neutrophil elastase, radiological involvement, and functional markers in a sample of 30 bronchiectasis patients (9). It was hypothesized that local or systemic antibiotic therapy and a consequent reduction in bacterial load reduce sputum NE levels. Previous findings suggest that short oral antibiotic therapy is effective in reducing NE activity in sputum (10-12). IL-8 is one of the most potent chemoattractants that degranulate neutrophils in the bronchiectatic airways. Long-term lung expression of IL-8 contributes to the double-edged sword of the inflammatory response in a variety of lung diseases,

including chronic obstructive pulmonary disease (COPD), bronchiectasis, and cystic fibrosis. Lung-targeted IL-8 provides enhanced protection against bacterial infection in the lung and leads to changes in inflammation, mucus hypersecretion, pulmonary remodeling and fibrosis, damaged and decreased lung function. Thus, IL-8-mediated enhanced microbial immunity presents with a high level of progressive lung injury and reduced lung integrity (13). It has also been suggested that IL-8 is a pro-inflammatory marker in bronchiectasis, COPD and allergic asthma IL-1 $\beta$  mediates airway inflammation and fibrosis (14,15). Recently, it was shown that transient expression of IL-1 $\beta$  using an adenoviral vector can lead to progressive fibrosis long after IL-1 $\beta$  levels fall and the acute inflammatory response has ended (16). Inhibition of IL-1 $\beta$  at the onset of animal fibrosis models has been reported to result in disease regression (17). Elastin degradation as a result of NE activity results in the presence of elastin-derived peptides, including desmosine and isodesmosine, in serum, plasma, and urine (18). Increased circulating desmosine in patients with bronchiectasis was also associated with a higher risk of severe exacerbations. Since few clinical parameters have been shown to be associated with bronchiectasis, sputum neutrophil elastase and circulating desmosine may be helpful in clinical trials or in patient evaluation (19). In another recent analysis in which 3 large studies evaluated bronchiectasis (TAYBRIDGE), COPD (ECLIPSE study), abdominal aortic aneurysm (MA3RS trial), high circulating plasma desmosine level has been associated with increased mortality in all causes of mortality independent of the underlying disease process and has been suggested to be a useful universal prognostic biomarker in populations at risk (20).

In this study, in patients diagnosed with bronchiectasis clinically and radiologically (with high resolution computed tomography), we determined NE activity in blood and sputum, diagnostic value of blood desmosine and proinflammatory biomarker (IL-8, IL-1 $\beta$ ) levels, correlations with symptoms, radiological extent, type of bronchiectasis, frequency of exacerbation, as well as sputum cell count and culture and aimed to investigate whether these biomarkers can be reliable markers in the diagnosis and follow-up of bronchiectasis.

## PATIENTS AND METHODS

The study consisted of 46 patients with

bronchiectasis, aged 18-90 years, whose last 5-year follow-ups (PA chest X-ray, HRCT) could be accessed, and as a control group, who were followed up by our Medical Faculty Hospital Chest Diseases Clinic and admitted between november 2020 and march 2021, and 45 people who applied to the chest diseases outpatient clinic for reasons other than bronchiectasis, without any cardiopulmonary, metabolic, cancer, acute or chronic inflammatory disease. This study was conducted in accordance with the Declaration of Helsinki, and the study approval was obtained from the Non-Invasive Clinical Research Ethics Committee of Medical Faculty (Decision No: 2019/2083). Written and informed consent statements were obtained from all participants. The patients' exacerbation frequency, cough, sputum production, shortness of breath, chest pain and hemoptysis histories were questioned. By measuring the NE level in the sputum of the patients, NE, desmosine, IL-8 and IL-1beta levels in the serum of the patients, these biomarkers were measured for the duration of the disease, symptoms, extent of the disease (radiologically involved lobes and segments), bronchiectasis type, exacerbation frequency, frequency of hospitalization, smoking history and sputum cell count and their relationship with bacteria grown in culture, and the correlation of biomarkers among themselves were investigated. NE, desmosin, IL-8, IL-1beta levels in the blood were studied. Blood and sputum samples were taken from the patients upon admission to the hospital, before the start of treatment. Not all sampled patients were receiving oral corticosteroids or any antibiotic therapy.

In order to investigate the correlation of the biomarkers to be studied with the radiological extent of the disease and the frequency of exacerbations, the routine laboratory tests (hemogram and CRP), thorax CT and/or high resolution lung tomography (HRCT) of the patients in their 5-year retrospective follow-up were examined, and their reports were scanned and recorded from the hospital information system. Disease duration, smoking history, symptoms, frequency of exacerbations and hospitalizations, and additional diseases were recorded by questioning the patients. Sputum NE, serum NE, desmosin, IL-8 and IL-1 were analyzed by enzyme linked immunosorbent assay (ELISA) method in the study. When gram stained preparations made from sputum samples were examined under the microscope, samples containing less than 10 epithelial cells and more than 25 leukocytes in each area at 100 magnification were accepted as suitable sputum samples. Eosin

methylene blue (EMB), chocolate agar and sheep blood agar medium were used for culture study of sputum samples. Identification of microorganisms thought to be causative was done by conventional methods, with automated systems when necessary.

The blood samples were centrifuged at 4 °C, 1,000 g for 10 minutes in a Hettich Rotina 46R (Hettich Zentrifugen, Tuttlingen, Germany) refrigerated centrifuge device, and serum samples were separated. Serum samples were stored at -80 °C in a New Brunswick U570 (New Brunswick Scientific, New Jersey, USA) refrigerator until the levels of IL-1 beta, IL-8, desmosine and neutrophil elastase in the serum were studied. Sputum samples were stored in a New Brunswick U570 (New Brunswick Scientific, New Jersey, USA) refrigerator at -80 °C until NE levels in sputum were studied. BT-Lab (E0890Hu, Bioassay Technology Laboratory Inc., Shanghai, China) kit was used for measurement of serum neutrophil elastase level. Neutrophil elastase results were calculated as "ng/mL" according to absorbance-concentration calibration charts using the Bio-rad microplate absorbance reader xMark (Bio-rad Laboratories, California, USA) system. The sputum sample was weighed and vortexed by adding four solids (w/v) 0.1% dithiothreitol. Four times (w/v) of the weighed sputum sample was vortexed by adding 0.9% NaCl (Sputum/DTT/SF ratio was 1/4/4 as w/v/v, dilution factor was 9). The mixture was centrifuged in a Hettich Rotina 46R instrument at 4 °C at 10,000 g for 10 minutes. Supernatant was used for the measurement of neutrophil elastase level.[21, 22] BT-Lab (E0890Hu, Bioassay Technology Laboratory Inc., Shanghai, China) kit was used for measurement of sputum neutrophil elastase level Neutrophil elastase results were calculated as "ng/mL" according to absorbance-concentration calibration charts using the Bio-rad microplate absorbance reader xMark (Bio-rad Laboratories, California, USA) system. AndyGene (AD10775Hu, AndyGene Biotechnology, Beijing, China) kit was used to measure serum IL-1 $\beta$  level. IL-1 beta results were calculated as "pg/mL" according to absorbance-concentration calibration charts using the Bio-rad microplate absorbance reader xMark (Bio-rad Laboratories, California, USA) system. For measurement of serum IL-8 level, USCN (SEA080Hu, USCN Life Science. Inc., Wuhan, Çin)) kit was used. IL-8 results were calculated as "pg/mL" according to the absorbance-concentration calibration charts using the Bio-rad microplate absorbance reader xMark (Bio-rad Laboratories, California,

USA) system. The MyBioSource (MBS771228, MyBioSource Inc, California, USA) kit was used for measurement of serum desmosine level. Desmosine results were calculated as “ng/mL” according to the absorbance-concentration calibration charts using the Bio-rad microplate absorbance reader xMark (Bio-rad Laboratories, California, USA) system. Pregnant women, patients who did not accept to participate in the study, and patients with acute or chronic infection or inflammation, except for ronsiectasis, were excluded from the study.

#### **Statistical Analysis:**

The results of our study were analyzed with the SPSS (The Package for Social Sciences) 19.0 program. The conformity of the data to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). In the evaluation of numerical data, arithmetic mean, standard deviation, median, minimum and maximum values were used and frequency distributions and percentages were used to summarize categorical data. Chi-square ( $\chi^2$ ) test was used to compare categorical data. The relationship between normally distributed numerical data and categorical data was evaluated with the T test in independent groups, and the relationship between non-normally distributed numerical data and categorical data was evaluated with the Man-Whitney U test. Correlations of non-normally distributed numerical variables were analyzed with the Spearman correlation coefficient. Diagnostic decision-making properties of IL-1 $\beta$ , IL 8, Desmosine and blood neutrophil/elastase levels in predicting the disease were analyzed by ROC (Receiver Operating Characteristics) curve analysis. In the presence of significant breakpoints, the sensitivity, specificity, positive predictive value and negative predictive values of these limits were calculated. Type-1 error level was accepted as 5% for statistical significance. In the evaluation of Spearman correlation coefficients, 0.05-0.30 was considered a low or insignificant relationship, 0.30-0.40 a low-moderate relationship, 0.40-0.60 a moderate relationship, 0.60-0.70 a good relationship, a 0.70-0.75 a very good relationship, and 0.75-1.00 an excellent relationship. Correlation coefficients with positive signs indicate that the variables increase and decrease together, while correlation coefficients with negative signs indicate that while one of the variables increases, the other decreases or vice versa (23). We calculated a sample size of 27 in each group with an

alpha error of 5% and power of 95.

## **RESULTS**

In our study, out of 46 bronchiectasis patients, 19 (41.3%) were female, 27 (58.7%) were male, and in the control group, 18 (40%) of 45 patients were female and 27 (60%) were male. The mean age of the patients with bronchiectasis was 50.56 $\pm$ 15.31 years. Active symptoms were present in 44 (95.7%) patients with bronchiectasis. Dyspnea and cough were present in 31 (67.4%), expectoration in 37 (80.4%) and hemoptysis in 2 (4.3%). Cystic bronchiectasis was found in 23 (50%) of the bronchiectasis patients, tubular bronchiectasis in 22 (47.8%), and varicose bronchiectasis in 1 (2.2%). 37 (80.4%) of 46 patients were able to produce sputum. In the microscopic examination of sputum, neutrophil dominance was observed in all samples. There was growth in culture in 9 (24.3%). *P. aeruginosa* was grown in 4 patients (44.4%), *enterobactericea* in 3 (33.3%), *acinetobacter baumannii* in 1 (11.1%) and *klebsiella* in 1 (11.1%). When their etiology was examined, etiology of unknown (idiopathic) was 21 (45.7%), childhood lower respiratory tract infection was 14 (30.4%), previous pneumonia was 6 (13%) childhood measles infection was 3 (6.5%), and previous tuberculosis was 2 (4.3%). Among the studied biomarkers, IL-1 $\beta$  (4.82 $\pm$ 3.09 - 2.03 $\pm$ 1.39,  $p < 0.001$ ), desmosine (0.71 $\pm$ 0.54 - 0.45 $\pm$ 0.12,  $p < 0.001$ ), blood neutrophil elastase (17.93 $\pm$ 8.11-10.29 $\pm$ 2.98,  $p < 0.001$ ), CRP (21.53 $\pm$ 43.25 - 2.88 $\pm$ 4.20,  $p = 0.003$ ) and blood neutrophil count (5.59 $\pm$ 2.52 - 4.47 $\pm$ 1.71,  $p = 0.026$ ) were statistically significantly higher in the bronchiectasis patient group. Sputum NE value in the patient group was 31.68 $\pm$ 17.00 ng/mL (Table 1).

There was no statistically significant difference in IL-1 $\beta$ , IL-8, desmosine, blood NE, sputum NE levels according to the etiology of bronchiectasis patients. The data are shown in (Table 2).

In order to determine whether IL-1 $\beta$ , IL-8, desmosine, blood NE, sputum NE values changed according to the etiology of bronchiectasis, a comparison was made between them; no significant difference was found.

It was investigated whether there was a difference in IL-1 $\beta$ , IL-8, desmosine, blood NE, sputum neutrophil elastase values in patients with bronchiectasis between those with and without symptoms. No significant statistical difference was found.

When the IL-1 $\beta$ , IL-8, desmosine, blood NE and sputum NE levels of the patients were compared

**Table 1.** Comparison of biomarkers, CRP and hematological parameters between patients with bronchiectasis and control groups

	Patients with Bronchiectasis n:46		Control Group n:45		p
	Mean±SD	Min-max	Mean±SD	Min-max	
IL-1β (pg/mL)	4.82±3.09	1.94-14.86	2.03±1.39	0.57-5.36	0.000*
IL-8 (pg/mL)	173.58±187.13	8.80-662.5	116.95±101.44	13.50-289.20	0.284*
Desmosine (ng/mL)	0.71±0.54	0.33-3.29	0.45±0.12	0.18-0.67	0.000*
Blood NE (ng/mL)	17.93±8.11	5.60-34.40	10.29±2.98	4.90-15.90	0.000**
CRP	21.53±43.25	0.00-235.0	2.88±4.20	0.00-23.00	0.003*
WBC	8.39±2.87	3.14-16.82	7.95±2.29	4.76-14.01	0.531*
Blood Neutrophil	5.59±2.52	2.25-12.87	4.47±1.71	2.43-10.30	0.026*
Blood Lymphocyte	1.99±1.04	0.38-5.03	2.76±0.93	0.88-4.56	0.000*
Sputum NE (ng/mL) (n:37)	31.68±17.00	10.46-73.68			

IL-1β: Interleukin 1beta, IL-8: Interleukin-8, NE: Neutrophil elastase, n: Number of patients, \*=Mann Whitney-U test, \*\*=independent samples t-test

**Table 2.** Correlation of CRP, WBC, neutrophil, lymphocyte counts, radiological involvement grades, exacerbation frequency, number of hospitalizations and smoking history of patients with bronchiectasis with biomarkers.

	IL-1β	IL 8	Desmosine	Blood NE	CRP	WBC	Blood Neutrophil	Blood Lymphocyte	Affected Lobe	Exacerbation	Hospitalization	Smoking History	Sputum NE
Disease period	0.188	-0.172	0.225	0.253	0.252	0.244	0.204	0.048	0.324*	0.770**	0.399**	-0.145	0.146
p	0.212	0.253	0.133	0.090	0.091	0.102	0.173	0.751	0.028	0.000	0.006	0.543	0.387
IL-1β		0.033	0.964**	0.899**	-0.071	-0.040	-0.074	-0.033	0.201	0.310*	0.050	-0.072	0.876**
p		0.827	0.000	0.000	0.640	0.790	0.626	0.828	0.181	0.036	0.739	0.763	0.000
IL 8			-0.053	-0.061	-0.059	0.074	-0.004	0.079	-0.098	-0.021	-0.091	-0.079	0.042
p			0.727	0.687	0.696	0.626	0.977	0.603	0.516	0.890	0.548	0.739	0.807
Desmosine				0.944**	-0.113	-0.057	-0.083	-0.046	0.244	0.328*	0.096	-0.030	0.922**
p				0.000	0.453	0.705	0.583	0.764	0.102	0.026	0.525	0.900	0.000
Blood NE					-0.224	-0.047	-0.091	0.000	0.146	0.316*	0.032	0.088	0.982**
p					0.135	0.756	0.547	0.998	0.334	0.032	0.835	0.711	0.000
CRP						0.394**	0.556**	-0.433**	0.277	0.324*	0.447**	-0.094	-0.275
p						0.007	0.000	0.003	0.062	0.028	0.002	0.693	0.100
WBC							0.895**	0.273	0.196	0.332*	0.207	0.361	-0.002
p							0.000	0.067	0.192	0.024	0.167	0.118	0.989
Blood Neutrophil								-0.090	0.252	0.287	0.242	0.452*	-0.084
p								0.551	0.091	0.053	0.105	0.045	0.620
Blood Lymphocyte									-0.102	0.014	-0.191	-0.098	0.155
p									0.502	0.926	0.204	0.680	0.360
Affected Lobe										0.509**	0.547**	-0.010	0.048
p										0.000	0.000	0.965	0.777
Exacerbation											0.692**	0.063	0.246
p											0.000	0.791	0.143
Hospitalization												0.067	-0.044
p												0.780	0.796
Smoking history													-0.133
p													0.636

IL-1β: Interleukin 1beta, IL-8: Interleukin-8, NE: Neutrophil elastase, \* p <0.05, \*\*p <0.01

**Table 3.** ROC analysis parameters of IL-1β, IL-8, desmosine and blood NE in patients with bronchiectasis

Biomarkers	AUC (Area under the curve)	95% Confidence Interval	p
IL 1β	0.832	0.747-0.916	0.000
Desmosine	0.717	0.514-0.821	0.000
Blood NE	0.786	0.688-0.884	0.000
IL 8	0.565	0.446-0.685	0.284

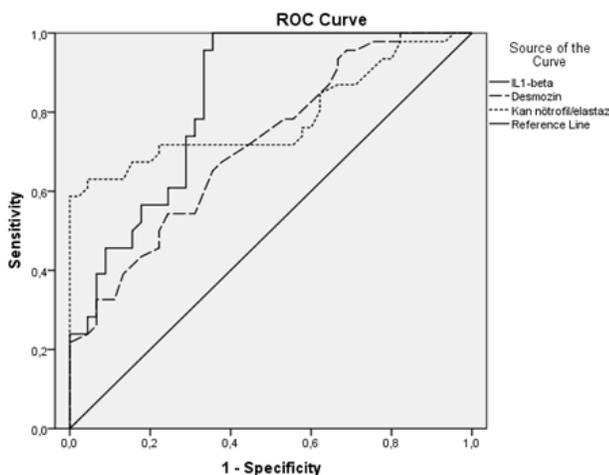
**Table 4.** Cut-off values, sensitivity, specificity, PPD and NPDs for IL-1 $\beta$ , desmosine and blood NE

Biomarkers	Cut-off value	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %
IL-1 $\beta$	2.935 pg/mL	73.9	71.1	72.3	72.7
Blood NE	12.70 ng/mL	71.7	77.8	76.7	72.9
Desmosine	0.505 ng/mL	67.4	62.2	64.6	65.1

IL-1 $\beta$ : Interleukin 1 $\beta$ , NE: Neutrophil elastase

according to the bronchiectasis type, no statistically significant difference was found between them. ROC analysis was performed to determine the diagnostic value, sensitivity, specificity, positive and negative predictive values of IL-1 $\beta$ , IL-8, desmosine, and blood NE (Table 3).

The cut-off value was not calculated for IL-8, since the AUC (Area under the curve) value was found to be insignificant (Figure 1). When the cut-off value for IL-1 $\beta$  was taken as 2.935 pg/mL in the diagnosis of bronchiectasis, its sensitivity was 73.9%, specificity was 71.1%, positive predictive value (PPD) was 72.3%, and negative predictive value (NPD) was 72.7%. When the cut-off value for desmosine was 0.505 ng/mL, the sensitivity was 67.4%, specificity was 62.2%, PPD was 64.6%, NPD was 65.1%. When the cut-off value for blood NE was taken as 12.70 ng/mL, the sensitivity was 71.7%, the specificity was 77.8%, PPD was 76.7%, and NPV was 72.9% (Table 4). No significant cut-off value with high sensitivity and specificity was found for IL-8 level, one of the parameters studied.



**Figure 1.** ROC curves for IL-1 $\beta$ , desmosine, and blood NE

## DISCUSSION

Neutrophils play a key role in the development and progression of bronchiectasis (24). Patients with clinically stable bronchiectasis also exhibit a persistent neutrophilic activation in the airways and have higher levels of sputum NE and other inflammatory mediators in the airways than healthy subjects (25). In our study, neutrophil dominance was detected in all sputum (100%) of patients with bronchiectasis. Also, blood neutrophil count ( $p=0.026$ ) and CRP value ( $p=0.003$ ) were found to be statistically significantly higher and blood lymphocyte count ( $p<0.001$ ) lower in patients with bronchiectasis than the control group.

According to our literature review, there are few previous studies on serum levels of NE. Most publications have investigated sputum neutrophil elastase. Our study was conducted with sputum NE, serum NE, IL-1 $\beta$ , IL-8 and desmosin in patients with bronchiectasis; and this is the most comprehensive study investigating the disease duration, exacerbation frequency, frequency of hospitalization, CRP levels, relations with WBC, neutrophil and lymphocyte counts, whether they vary according to the number of affected lobes and segments and bronchiectasis types, whether they differ according to their etiology, whether they are affected by the history of smoking, whether they vary according to the bacteria that reproduce in the sputum and correlations of these biomarkers with each other.

In our study, serum NE levels were found to be statistically significantly higher in patients with bronchiectasis than in the control group ( $p<0.001$ ). The diagnostic value of blood NE level in predicting bronchiectasis was analyzed by ROC analysis. When the cut-off value was taken as 12.70 ng/mL; it was observed that it had high sensitivity (71.7%), specificity (77.8%), positive predictive value (76.7%) and negative predictive values (72.9%). A statistically significant positive correlation was found between the blood NE level and the number of exacerbations in bronchiectasis patients ( $p=0.032$ ,  $r=0.316$ ). A statistically significant positive correlation was found

between blood NE level and sputum NE level ( $p=0.000$ ,  $r=0.982$ ).

IL-1 $\beta$  was found to be much more expressed in the airways of children with prolonged bacterial bronchitis (USBB) and bronchiectasis, a precursor to bronchiectasis in some children, compared to the control group, and this was significantly associated with clinical outcomes. This observation has been found not only in children, but also in adults with chronic respiratory disease, where elevated IL-1 $\beta$  is associated with poor lung function and the presence of pathogenic bacteria in non-CF bronchiectasis (26). Chen et al. reported that IL-1 $\beta$  may be a therapeutic target in these conditions, given that high IL-1 $\beta$  concentration is highly correlated with symptom severity, disease recurrence, and intensity of airway inflammation (27). In our study, IL-1 $\beta$  level was found to be statistically significantly higher in patients with bronchiectasis than in the control group ( $p<0.002$ ). Similar to previous clinical studies, a statistically significant positive correlation was found between IL-1 $\beta$  and the number of exacerbations ( $p=0.036$ ,  $r=0.310$ ). ROC analysis was performed to determine the diagnostic value of blood IL-1 $\beta$  level in predicting bronchiectasis disease. When the significant cut-off value was taken as 2,935 pg/mL, high sensitivity (73.9%), specificity (71.1%), positive predictive value (72.3%) and negative predictive values (72.7%) were found similar to NE.

Excessive lung elastin degradation results in increased blood levels and urinary excretion of elastin-derived peptides such as desmosine and isodesmosine (28). Desmosin is a structural amino acid that is specifically released into the circulation when mature elastin is broken down (29). In our study, blood desmosine level was found to be significantly higher in patients with bronchiectasis than in the control group ( $p<0.001$ ). In the analysis made with ROC analysis, when the cut-off value was 0.505 ng/mL; sensitivity was 67.4%, specificity was 62.2%, positive predictive value was 64.6%, and negative predictive value was 65.1%. In the study of Chalmers et al., desmosine level was correlated with sputum elastase ( $r=0.42$ ;  $P<0.0001$ ). In this study, it was reported that blood desmosine was a good marker of sputum elastase activity and was confirmed to be associated with severe exacerbations of bronchiectasis (19). In our study, in addition to a statistically significant positive and excellent correlation between blood desmosine level and sputum neutrophil elastase ( $p<0.001$ ,  $r=0.922$ ), there was also a statistically significant

positive excellent correlation between desmosine and blood NE ( $p<0.001$ ,  $r=0.944$ ). At the same time, a statistically significant positive correlation ( $p=0.026$ ,  $r=0.328$ ) was found between the desmosine level and the number of exacerbations. Polverino et al. reported that because exacerbations are a very important prognostic factor in bronchiectasis, desmosin can be used to select patients with frequent exacerbations who may benefit from antielastase therapy (30).

Overexpression of IL-8 in the bronchial epithelium has been shown to benefit lung immunity against bacterial infection, but specifically leads to impaired lung function by causing lung injury through persistent inflammation, lung remodeling, and damaged tight connective tissues (13). In the study of Ayhan et al., the serum IL-8 level of the patient group in patients with stable bronchiectasis was found to be statistically significantly higher than the control group ( $P=0.001$ ). In this study, it was reported that IL-8, an inflammatory cytokine, was found to be correlated high in both serum and BAL. These significant findings and correlation suggested that bronchial inflammation continued in patients who were not in the exacerbation period. This has led to the thought that bronchial tissue damage continues in different localizations and in different intensities as long as the inflammation continues. Although the physiological significance of high IL-8 levels in the stable period of bronchiectasis cases is not fully known, it was reported to support the fact that inflammation continues and the systemic cellular response is active even in stable periods (31). Bergin et al. detected high levels of IL-8 in airway samples taken from patients with bronchiectasis without cystic fibrosis. It was stated that the presence of high IL-8 levels supports the use of appropriate anti-inflammatory therapies (32). In our study, blood IL-8 levels were higher in patients with bronchiectasis than in the control group ( $173.58\pm187.13 - 116.95\pm101.44$ ,  $p=0.284$ ), but no statistically significant difference was found. Angrill et al. showed that airway inflammation is persistent in patients with bronchiectasis, and NE and other inflammatory mediators were higher in the bronchoalveolar lavage (BAL) of 23 patients, even in the absence of bacterial colonization, compared with healthy subjects (33). Previous studies have reported that purulent sputum is associated with NE concentration and can be considered as a marker for proteolytic and inflammatory activity. Moreover, NE has been shown to increase progressively with increasing bacterial load in sputum. Chalmers also reported a strong association between sputum

bacterial load and a range of inflammatory mediators in a cohort of 434 bronchiectasis patients (25). In our study, 37 of the patients with bronchiectasis had the complaint of active sputum production, and the mean NE value in the sputum sample of these 37 patients was measured as  $31.68 \pm 17.00$  ng/mL. In other biomarkers examined by sputum neutrophil elastase level; a statistically significant and excellent positive correlation was found between blood NE, desmosine and IL-1 beta. There was no significant correlation between sputum NE and bacterial load and type, probably due to the low number of patients who could give sputum samples and the low number of bacteria grown in sputum. In our study, when sputum NE levels were compared according to bronchiectasis type, it was found that patients with cystic bronchiectasis ( $37.52 \pm 18.86$  ng/mL) were higher than those with tubular bronchiectasis ( $26.14 \pm 13.26$  ng/mL). It was not statistically significant, but it had a p value very close to significance ( $p=0.054$ ).

Besides, in our study, a statistically significant correlation was found between the number of exacerbations and the number of affected lobes and segments in the patient group with bronchiectasis ( $p < 0.001$ ). Again, a statistically significant correlation was found between the number of affected lobes and segments and the number of hospitalizations ( $p < 0.001$ ,  $p = 0.003$ , respectively). These relationships show that the number of affected lobes and segments of the patient increases as the number of exacerbations and the number of hospitalizations increase, in accordance with Cole's vicious cycle in the pathogenesis of bronchiectasis, while the frequency of exacerbations and hospitalizations increases as the involved lung section increases (34).

## COCLUSIONS

In our study, it was observed that NE, IL-1 $\beta$  and desmosine in the blood of patients with bronchiectasis were significant inflammatory markers that were significantly higher than the control group, had significant diagnostic value, and could be an important component of the diagnosis and follow-up parameters since these parameters were significantly correlated with the frequency of exacerbations. The excellent positive correlation of NE in sputum with these three biomarkers suggested that it may be a strong candidate for routine follow-up parameters. In particular, blood NE and IL-1 $\beta$  stand out as very valuable parameters that should not be ignored in the follow-up of the disease, with the highest sensitivity,

specificity, NPD and PPD values. Further studies are needed to evaluate the contribution of blood NE, IL-1 $\beta$  and desmosine in determining the etiology of bronchiectasis, its relationship with symptoms, its relationship with bacteria isolated in sputum culture, and their correlation with bronchiectasis types.

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# Cognitive Therapy in Rumi's Works

## Mevlana'nın Eserlerinde Bilişsel Terapi

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### Öz

Biyopsikososyal bir varlık olan insanın, psikolojik sorunlarını anlamak ve iyileşme sürecine katkı sağlamak için kültürel ve dini öğelerden de yararlanılabilir. İnsanlık tarihinin başlangıcından beri mental sorunlar var olduğu için iyileştirici ve dayanıklılığı artırıcı öğretiler geliştirilme çabaları da olmuştur. Bazı öğretilerin yerel kalmasına karşın tüm insanlara etki edebilecek ve ortak hazinemiz olarak kabul edilebilecek birçok öğe de mevcuttur. Mevlâna, Anadolu ile özdeşleşmiş ama evrensel olarak bilinen bir mistik, felsefeci, şair ve düşünürdür. Eserlerinde yaşadığı yüzyılın dini yaşantısı ve düşünce dünyasına katkıları gibi insanın ruhsal yapısını da ilgilendiren gözlem ve tespitlerde bulunan bir kişidir. Dünyada en yaygın kullanılan ve hakkında bilimsel araştırmaların yapıldığı terapi yöntemi Bilişsel Davranışçı Terapidir. Bilişsel kurama göre kişi karşılaştığı nesnel durumu, mevcut bilişsel alt yapısı nedeniyle çarpıtır. Bu çarpıtma sonucunda ortaya çıkan otomatik düşünceler, işlevsiz bir takım duyguların ve çoğunlukla bu duygularla ilişkili davranışların ortaya çıkmasını sağlar. Rumi'nin eserlerinde düşünce-duygu ve davranış ilişkisini vurgulayan ve çeşitli ruhsal sıkıntılardan kurtulmak için farkındalık ve bilişsel değişimi öneren birçok tavsiyeler yer almaktadır. Bu gözden geçirmede Mevlana'nın eserleri Mesnevi, Fihi-Ma-Fih, Divan-ı Kebir, Mektubat ve Mecalis-i Seba taranarak bilişsel kuram açısından irdelenmiştir. Rumi'nin şiirlerinde, kullandığı öykülerde birçok bilişsel kuramla ilintili öğeler olduğu ve bunun psikoterapi uygulayıcılar tarafından danışanların dayanıklılığını artırmak ve bilişsel değişimleri için kullanılabileceği düşünülmüştür.

**Anahtar Kelimeler:** Mevlana, bilişsel terapi, düşünce

### Abstract

Cultural and religious elements can also be used to understand the psychological problems of the human being, who is a biopsychosocial being, and to contribute to the healing process. Since mental problems have existed since the beginning of human history, there have been efforts to develop healing and resilient-enhancing teachings. Although some teachings remain local, there are many elements that can affect all people and can be considered as our common treasure. Mevlana is a mystic, philosopher, poet and thinker who is identified with Anatolia but is universally known. In his works, he is a person who makes observations and determinations concerning the spiritual structure of humanregarding the religious life of the century he lived in and his contributions to the world of thought. The most widely used and scientific research carried outtherapy method in the world is Cognitive Behavioral Therapy. According to the cognitive theory, person distorts the objective situation he encounters due to his current cognitive infrastructure. The automatic thoughts that arise as a result of this distortion lead to the emergence of a number of dysfunctional emotions and behaviors often associated with these feelings. Rumi's works contain many recommendations that emphasize the relationship between thought-emotion and behavior and suggest awareness and cognitive change to get rid of various mental distresses. In this review, Rumi's works were examined in terms of cognitive theory by scanning "Masnawi", "Fihi-Ma-Fih", "Divan-ı Kebir", "Mektubat" and "Mecalis-i Seba". Rumi's poems and the stories he used were thought to have elements related to many cognitive theories and that this could be used by psychotherapy practitioners to increase the resilience of clients and to change their cognition.

**Key words:** Rumi, Cognitive therapy, thought

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## INTRODUCTION

Human is a biopsychosocial being. As well as having an impact on the development of the physical elements of the geography where was borned and lived, the cultural, religious beliefs and social variables of the society are also effective in its spiritual development. Mental health professionals must comprehensively assess their biological, psychological, and social areas to understand and help their patients. Therapy interventions should also cover these issues (1). Many factors such as cultural, religious, and social, can be used in understanding psychosocial factors and utilizing them for treatment. It is important for effective therapy that the therapist learns the social and religious elements that are beneficial to mental health in the society in which he lives. Today, cultural and mystical elements appear to be effective in cognitive therapy and subsequent acceptance-commitment and mindfulness-based therapies (2-4). In this regard, it is thought that the examination of Rumi's works in the perspective of cognitive theory, for whom we can use the definitions such as mystic, philosopher and poet, identified with Anatolia but universally known, will contribute to the field.

Mevlana Jalaluddin Rumi was born in Balkh in 1207 and spent his childhood there. The city of Balkh has been the capital of more than one civilization throughout history as it was established on the main trade routes connecting India to the north and east due to its strategic location. At the same time, in Balkh, one of the socioeconomic and religious centers of Khorasan, people of different races, religions and sects lived together, and so created a rich cultural and religious mosaic. Balkh is considered as one of the centers of Zoroastrianism, Buddhism, Hellenism and Melamiteness. Rumi's first teacher was his father, Muhammad Bahâeddin Walad (5). The teachings of a father who was fed by this mosaic and his own nourishment of this cultural richness were effective in Rumi's creation of ideas that could be adopted all over the world and used in different disciplines. With the religious life of the century, he lived in and tis contributions to the world of thought; Rumi is a person who makes observations and determinations that also concern the spiritual structure of human. For this reason, he has reached a widespread readership all over the world and UNESCO declared the year 2007 as the year of Rumi and described him as an "Eminent philosopher and mystical poet of Islam who advocated tolerance, reason and access to

knowledge through love. His mystical relationship to Islam produced masterpieces that well beyond the borders of Turkey has marked Islamic culture and devotion" (1).

Aeron Temkin and Albert Ellis is considered as founders of cognitive therapy, which is currently one the the most widely utilized psychotherapy methods. In this model, thought has a central role in depression, anxiety, and other emotional changes and in the persistence of these emotions (6). Beck's cognitive model suggests that there are many levels of cognitive assessment. According to the cognitive model, in the case formulation, the person distorts the "objective situation" encountered due to the current cognitive infrastructure. The "automatic thoughts" that emerge because of this distortion lead to the emergence of several dysfunctional emotions and behaviors often associated with these emotions (7,8). In cognitive therapy, it is suggested that the therapy should be focused on the thoughts and beliefs of the individual, since people have the potential to eliminate and reduce the impact of experiences by commenting on their experiences and thinking about them (8). In Mevlana's works, there are many recommendations that emphasize the relationship between thought, emotion, and behavior, suggesting awareness and cognitive change to get rid of various mental troubles. Unfortunately, the researches examining Rumi and his works in this context are almost none (1-4).

Mevlana's works were examined regarding cognitive therapy by scanning "Masnavi", "Fihi-Ma-Fih", "Divan-ı Kebir", "Mektubat" and "Mecalis-i Seba" (9-11). In particular, it was tried to determine his comments on thought and his stories that could be interpreted in the context of cognitive therapy.

## RESULTS AND DISCUSSION

When the works of Rumi were examined, there were no elements that could be associated with cognitive theory in the content of "Mektubat" and "Mecalis-i Seba". The findings of the remained three works by dividing them into subheadings were presented below.

### **Cognitive conceptualization**

The cognitive theory is defined as; the meanings we give to ourselves, the outer world and to other people, our thoughts, our rules, our expectations, our basic beliefs affect how we perceive the events we experience, how we react to what we experience and how we feel.

*"The Indians wanted to bring an elephant to a*

*dark barn and show it to the people. A lot of people gathered in that dark place to see the animal. But the barn was so dark that there was no way to see it with the eye. In this darkness they began to rub their hands on the elephant. Someone got his ear in his hand and said, 'The elephant looks like a fan.' The other had a tornado in his hand and said, "The elephant looks like a trough." Someone else had his leg in his hand, and he said, "The elephant looks like a pole. Another one groped his back and said, "The elephant is like a throne." Wherever everyone thought they were, they set out to explain the elephant accordingly. Their words were contradictory because of their views. One said dal, the other elif. If everyone had a candle in their hands, there would be no contradiction in their words." (Masnawi, 1259, c3)* In this story, which beautifully metaphorizes the difference in perception and interpretation in cognitive conceptualization, each person sees and defines the elephant according to his own narrow mental framework.

In cognitive conceptualization, thoughts are defined at the surface, but the deeper schema (basic belief) and intermediate beliefs consisting of rules, assumptions and attitudes that develop in relation to them are also important in cognitive intervention in formulation. As if to describe this structure, Mevlana stated the following. *'The root was hidden, it came out. Know your narrowness and spaciousness as a root. If it's a bad root, remove it quickly so that an ugly thorn doesn't grow on the lawn. When you see your inner distress, find a cure for it. Because the branches always consist of roots. When you see the width, water it, and when it grows and bears fruit, distribute it to the friends (Masnavi, c3, 360)* Here the roots can be similed as the basic belief, the branches to intermediate beliefs, and the flower or thorn thoughts on the surface. In fact, it can be considered as an analogy that describes the strengthening of positive core beliefs and the work on the negative.

#### **Automatic thoughts and cognitive interventions**

In cognitive theory, thoughts are defined as the cause of dysfunctional reactions, emotions, and often physiological symptoms (such as palpitations, sweating, tremors). At the beginning of the therapy process, the person's awareness of these thoughts is ensured. Then, by changing the non-functional ones, they are taught by experiencing that their distress will begin to decrease, their dysfunctional behaviors will also decrease, and their physiological arousal responses will return to normal (12,13). When Mevlana's works are examined, it is noteworthy that

there are many definitions that overlap in the context of cognitive theory: *Brother, you are only that thought, that spirit. In terms of your faithful being, you are nothing but bone and skin. If your thought, your spiritual being, laughs, you are the rose garden; you are worthy of a thorn. If you are rose water, they will drive you to the head and sprinkle you on your sheep; If you're like a sneak, they'll throw it out. (Masnawi, 275)*

*So many thoughts, thousands of delusions come to you; you fall into various states. None of them are in your hands, nor do they obey your command. If you knew the place of their birth, if you understood where they came from, you would multiply and decrease them as you wished. The passage of all this is in you, but where does it come from, where does it go; what to do; you don't know. (fi-imafif, p82). I hung thought on the gallows, because thought gives separation. I don't like the thought. I'm sick and tired of it. After all, I am always miserable because of reason, because of thought. (Divan-iKebir c3,1394). Suppose these visible images and bodies are a jug! See it like a jug! Dreams are the poisonous syrup in thoughts, in those jugs. We are all filled and empty with poisonous thoughts like a jug at any moment. (Divan-i Kebir c4,1652).* In the above definitions, we see the metaphorical narrative about the uncontrollability, effectiveness and negativity of thought. These definitions, which are sequelled below, seem to be compatible with the characteristics of automatic thinking in cognitive therapy.

*Bring the glass of fire that burns thoughts and anxieties and present it to me, because there are thoughts and sorrows in my head, brought by both hope and fear. (Divan-i Kebir, c2, 876). Let go of thought, of delusion; don't give them a place in your heart! For you are like a naked person; Thought is like the cold of the zemheri, protect yourself from the zemheri! You are caught up in the thought of getting rid of trouble, boredom, suffering! Of these, the thought that you hold onto is the source of misfortune and suffering. (Divan-i Kebir c,1122). Because of a single thought that comes to your heart, hundreds of worlds are overturned upside down in an instant. (Masnawi, 1025). Wherever your thought goes, it drags you along you and pulls you there. You give up thinking, walk forward like accident and destiny, get ahead! (Divan-i Kebir c5,2131). Why did you get stuck on a thought, you were helpless? Have you closed in on yourself, sunk into the scales? When you were in pieces, that is, when your material existence*

*was scattered in various places, when you were stuck with the elements, I gathered you together, why did you fall into delusion, you became a hundred pieces (Divan-i Kebir c6,2660)*

*Thou shalt give us thy chalice, let the soul be freed from thought, let it pass with, and let the water tear the curtains of self. Let him cast the thought aside. Because thinking beats the soul up and reduces the life span at any moment. (Divan-i Kebir, vol. III, 1382).* Rumi described in many places of his works that he had a lot of trouble because of thought and made suggestions in the form of cognitive intervention. For example, the following statement is thought to describe the formation of alternative thinking. *When a thought comes to your mind, know that there is the opposite of it! You are amazed by two opposing ideas and are caught up in the possibilities. (Divan-iKebir c6.3036)*

**He continues his recommendations as follows:**

*'He who frees his heart from the greed of the world and makes him comfortable makes the crocodile's back a ship for himself' (Divan-ı Kebir C2, 1322).*

*'When the soul unties the hands of the mind that are tied, he does the things that are impossible to do.*

*Thoughts and emotions have covered the face of clear water like garbage.*

*The hand of the mind throws them to one side, and water appears.*

*Garbage covers the face of the water like habbe... But when they are driven to one side, water appears.*

*Unless Allah opens the hand of reason, the air will fill the face of our water with garbage and sweepings" (Masnawi, 1825).*

*Come to your senses, wake up from the sleep of ignorance, get rid of the thought and the dream!.. (Divan-iKebir c5, 2538)*

*Thought becomes a veil to the moon face of the heart. The heart is like a moon. The thought becomes a cloud, covers it, hides its nourishment. For this reason, do not give place to the thought in the heart, throw the thought into the water! (Divan-iKebir, c5, 66).*

In this beautiful metaphorical narrative in Fihi-Ma-Fih, the automatic thoughts that are emphasized and first studied in cognitive therapy are symbolized as the 'captive army of thoughts'. He defined these negative thoughts, which often hinder man from revealing his potential, as an army to fight. In socially phobic patients, although there is often no inadequacy, on the contrary, even in an area where it is good, negative thoughts are often blocking. Again, obsessives are

actually like prisoners of these armies of thought. Here, Mevlana made an analogy that can be used in relation to similar situations, defined as captivity to thought. Gerçek suggested that the battle should be with the internal processes of the person, he paid less attention to external factors, and the cognitive area emphasized in therapy for change was emphasized.

"Almighty God has made these words our soldiers and an army to surround you, to see a mural between you and the enemy, to destroy the enemies, but the enemies within. External enemies are nothing; what could it be? Don't you see? So many thousand infidels were imprisoned by a single infidel with their sultan; if he is an infidel, he is a prisoner of his own thought. We get it, it's all about thinking. If so many thousand peoples, even the world, are imprisoned in a pure, a fuzzy thought, what will not happen there where eternal thoughts reign? Pay attention and see. That world has neither greatness nor supremacy; how it overwhelms its enemies, nor does it condemn the worlds. Because we see it clearly, hundreds of thousands of shapes, plains, armies full of writings, if we are captive to one person, that person is a prisoner of a vulgar, despicable thought. So all this is caught in one thought; alright; what great, lofty, holy eternal thoughts do not do; we get it that it is all about thinking. Shapes are always the means of thoughts, the means of thoughts; Didn't you think, they're all unemployed-powerless, they're all frozen, they're frozen to death . So the one who sees the shape is also frozen; no way of understanding; even if he is apparently old, even if he is found to be a hundred years old, he is a child, not an adolescent. "We have turned from the smallest war to the biggest war." We were fighting with shapes, with visible enemies; we are now fighting armies of thought; let good thoughts break bad thoughts, defeat them, remove them from the province of the body; that's why we went to war; that is the greatest war. In this war, thoughts are in the flesh-and-power without bodies. You know, the mind turns the sky without a tool and says that there is no harm to the vehicle, and here is it like him (Fihi-Ma-Fih, p22).

In the following phrase, Mevlana is thought to use the metaphor of negative automatic thoughts as 'poisonous nails' and in the subsequent statement he metaphorizes the effects of similar thoughts as leading to the loss of treasures that the person has.

*The purity and cleanliness of Nefsi Mutmainne is clouded with thoughts. As a matter of fact, you write something on the face of the mirror, or you do something, and then if you clean it, there will still be a*

*trace, a deficiency.*

*When the flesh falls on Nefsi Mutmainne's face, the nails hurt.*

*Know bad thought as poisonous nails. This nail scratches the face of life as it deepens.' (Masnawi, c5,555). 'You are losing the treasure because of what you think is treasure.*

*Know your delusions, precautions and thoughts well, there will be no treasure in prosperous places.*

*Being in prosperous places means striving. The one who disappears is ashamed of the beings and gets offended.*

*The being did not cry out of nothingness. Absence has removed that presence from itself.*

*Don't say, "I'm running away from nothing." In fact, he is running away from you twenty times more." (Masnavi C1, 2475)*

### **Cognitive distortions**

The part of automatic thoughts named as dysfunctional and negative thoughts, are a product of the cognitive process that occurs in our minds in relation to a situation and is not suitable for the situation. We call cognitive distortion that the mental processes that perceiving the fact not as it is, but in a different (distorting) way, leading to results that are not in line with reality (13). Let us give examples of cognitive distortions from Mevlana's works:

**What if:** *O thought; Enough is enough! In every breath; "I wonder what happened to him?" "Oh, what should I do with that and that?" don't worry about it! Beloved, he tells you everything! (Divan-i Kebir c4,2060).*

**Should statements:** *'O lovers! "It should have been so-and-so!" There are words like "This is how it will happen!" or these words have dragged the people into a pit! We got rid of these words, and we got rid of these thoughts." (Divan-i Kebir c 3, 1419).*

In the following story, Rumi mentioned there are cognitive distortions such as 'ignoring the positive aspect', 'catastrophizing', 'what if' and described those lead anxiety.

*There is a lush green island in the world, where a gluttonous ox lives alone. It licks the whole plain until the evening, weeds, gets full, gets fat and swells. When it is night, it thinks about what I will eat tomorrow, this thought makes it worry and turns it into a thin hair. In the morning, the plain blossoms again. Greenery, meadow, grass have grown to the waist. The ox is starved of oxen, it grazes the whole plain until the evening and ends it. Again it grows, fattens up, swells. Its body becomes fattened, it becomes strong. Then, in the evening, it falls into the fear of*

*hunger, begins to tremble with this fear, and again weakens from its fear. What will I eat tomorrow when grazing. What will I do? it keeps thinking. For years, that ox has been in this state. I've been weeding this greenery all these years, spreading it on this lawn. Not a day of sustenance diminished. It doesn't even think about what this fear is, what is this grief that burns my heart. It's evening, and when night comes, that fat ox will become weak again because it thinks it has run out of sustenance. Here is the nafs, it is the ox, and the plain is the world. The nafs will definitely weaken with the fear of bread. What will I eat in the future? The nafs worries about how and where I will get the sustenance of tomorrow. You've eaten for years, your food hasn't run out. Now let go of some future thinking and look at the past. Remember the sustenance you eat, don't look to the future, whine a little! (Masnawi, 2855-65)*

### **Obsessive Compulsive Disorder**

Among the patients diagnosed with Obsessive Compulsive Disorder, particularly those with autogenic obsessions (sexual, religious and aggressive content) are most disturbed by the arising of these obsessions their minds and blaming of themselves. Feeling responsible for these thoughts and trying not to think about them reveals the cycle of more thoughts being experienced and feelings of guilt increasing (13). It has been experienced that talking about Mevlana's views on this issue makes it easier for patients to internalize the lack of control of thoughts and that they are not responsible. The definitions in the chapter on the subject contain excellent metaphors for the cognitive paradigm:

*"No one can be responsible for thought. The man's interior is the world of freedom. For thoughts are invisible to the eye; judgment cannot be rendered on the basis of opinions. "We judge by outward appearances; God knows what's hidden" The thoughts of the Almighty God state in you; If you make hundreds of thousands of efforts, if you suffer with alas, you will not be able to take away thoughts from yourself. You know, they say, God doesn't need a tool; Don't you see, how you have these thoughts, without tools, without pencils, without shapes, without color. Thoughts are similar to birds flying in the air, gazelles roaming in the forest. Unless you catch the bird and put it in a cage, it is not right to sell it in the sharia; you cannot sell the bird in the air; you can't afford this: it is essential to give the thing sold to the buyer. You don't have what you can give? Thoughts are nameless as long as they remain within; you can't judge them, you*

*can't call them blasphemy, you can't call them Islam. Did the Kadi ever say that you confessed that, you made this kind of sale, come, swear that you didn't have that thought? He can't say; for no one can judge what has passed from the heart, what has come of memory. Thoughts are birds in the air. Now, when it comes to the word, it can be judged that it is blasphemy or Islam, good or bad at that moment.'* (Fihi-Ma-Fih, p38)

### **Social Anxiety Disorder**

The cognitive distortions in Social Anxiety disorder are that of oneself's inadequacy, the ruthlessness of the outer world, and the thought that other people are superior and critical (13). The following definition of Rumi is a metaphor that we bring to bear in practice within the sessions and in which the client experiences the effect of thoughts.

*'If there was a road half a cubit wide on the ground, a person would walk comfortably without any delusions. But if you go on a high wall, if the width of the road is still two cubits, you will go crooked. You may even fall because of the delusions that fall into your heart. Pay close attention to the fear of delusion and understand the evil of delusion'. (Masnawi, vol. III, 1558-1561)*

### **If the thought reflects reality:**

If the thought reflects an objective situation, in other words, if the cause of the person's pain and anxiety is actual, such as having cancer, going bankrupt or losing a child, the therapist should support the one firstly to accept the situation and afterwards should head for solutions or other options (endurance, activating support components and focusing on the normalization process, etc.). Acceptance means receiving what is offered. To experience events and situations as they are is to let them to happen. In addition, it also includes effectively embracing the thoughts, feelings and bodily sensation experiences that have arisen inside the person as they are (3,4). In his works, Rumi emphasized the growth in sorrow, purification and the gains of experience with the following definitions:

*Every day, the thought that comes to the heart is like the guest who comes in the morning on that day, dominates the host, makes him grumpy. The glory of being a host is to see and watch over the guest, to entertain him, and to attract his kindness. Just as a great guest comes to the guest house every day, an idea comes to you at every moment, just like him. My dear, consider the idea a man. Because the man is valuable with the idea, he is alive with the idea. Don't*

*be sad if the idea of grief hits your way to joy. He is really preparing other joys. He sweeps the house firmly from others so that a new joy, a new happiness may come from the truth of the good. (Masnavi 3655)*

*It separates the yellowed, dried leaves from the branch of the heart, helping to finish new and green leaves from the branch. It pulls the old joy from its roots so that a new pleasure can come to a world beyond this world. Grief uproots the old root, which is rotten and withered, so that it may devour the new root, which is covered with branches and leaves. Whatever grief spills or breaks from the heart, it will definitely give something better in return. Especially those who know well that troubles and sorrows are servants, will find more blessings. (masnavi 3680).*

*Since your beloved wants to see you in grief, do not seek joy anymore! O saintly hunt; you are between the two claws of the lion of love! If the beloved pours rose water on your head, accept that rose water as the musk of the Tatar land! There is a hidden enemy inside you! Nothing can drive that terrible enemy, that dog of nafs out of it, other than torment and suffering!*

*If someone keeps hitting the felt or the carpet with a stick, those sticks are not for beating the felt or carpet, but for removing dust! There are dusts of being, of self in you; those dusts, like carpet dust, do not go away with just a swipe! When trouble comes, when you are in pain, when you endure the troubles that happen to you, sometimes while you are sleeping, sometimes while you are awake, those dusts of grief fly away little by little without you noticing! If you don't want to sleep, if you run away from sleep, if sleep catches you and makes you sleep, you will see the suffering of your lover, the seemingly wrong works of that deva who achieved good deeds in your dreams! Carving the wood is not to destroy it; it is to adapt to the wishes of the carpenter! That is why all the evils in the way of Allah are good; its benevolence, its beauty, is finally revealed and seen! Don't you see; the plate keeps putting dirt on the hide; repeats this a thousand times! Its purpose is to reveal the hidden disease in the skin! The leather doesn't even know much about it, but what the plate wants is to clean the leather! Divan-i Kebir vol.III, 1139)*

It has been described that the sad events encountered, contribute to the mental strengthening of the individual in the journey of life and make them purify, mature and grow, and their temporariness is often emphasized. He emphasized that the events that are considered negative in sectional evaluation, can prevent greater negativities over time.

*If the cloud and lightning did not show sullen and sour faces, would the vine leaf ever show its east-like smiles? Happiness, unhappiness, comes to your heart, stays. They are like stars going from house to house. When he stays in your sign, you become sweet like his luck, become agile.(Masnavi, 3685).*

*The feelings in the heart should not remain in the heart for a long time. That is why, in expressing feelings, thoughts, there is a relief and relief for understanding. This state is like the flight of a prisoner bird in the heart. But, O bird of my heart, fly in secret; don't fly in plain sight! (Divan-iKebir, c5,2125)*

## RESULT

Human is a living being who lives in different parts of the World and who has many cultural and religious differentness in life as well as physical characteristics. Human beings suffer from physical diseases and mental problems that have various symptoms in the process of life. It is important to make common efforts to treat and prevent them. Of course, resilience is an important notion as well as treatment. Even if there is a pool of common knowledge and experience to increase both treatment and resilience, the richness and commonuse of this pool for mental problems is insufficient. Rumi's works are universal and comprehensive. Rumi has offered suggestions for the causes and solutions of many spiritual sufferings. He cared deeply about mental processes, thinking, and made suggestions for cognitive awareness and change. I have tried to present here the elements of these works, which thought to be written for all people, that can draw the attention of cognitive therapists and benefit from them, and I have tried to make a modest contribution to the pool of elements that would increase our common healing and resilience.

The main theme of cognitive therapy, automatic thoughts, explaining the power of their effect and metaphorical and understandable definitions in terms of cognitive conceptualization are exemplified in Mevlana's works. In terms of interventions in cognitive behavioral therapy, in Mevlana's works, we see examples that include many concepts such as the concept of automatic thought, the lack of control of thought, the lack of responsibility for thought, the relationship between emotion and thought, and the fact that thoughts can be consciously examined and changed. Although Mevlana lived about eight hundred years ago, he left works behind that inspired the psychotherapy movements of our time. Although it is not known how much cognitive therapy theorists are

influenced, the examples we have described above show the influence of Rumi in the concepts that form the fundamentals of cognitive therapy.

Since there are limited number of works on the subject, it couldn't discussed comparatively and the level of success of our effort in understanding and putting Mevlana and his works across can be shown among the limitations of the article. Moreover, as the works were analyzed in the context of cognitive therapy, Mevlana's general thought structure and deep tassavufi views were not included in this compilation. Mevlana and his works are not identified among the people and works influenced by the developers of cognitive therapy. This relationship has been claimed by us. The effort to establish a connection between cognitive theory and Mevlana may have led to the interpretations of mystically profound sayings to remain superficial.

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# Biliopleural Fistula Due to a Rare Liver Hydatid Cyst

## Nadir Görülen Karaciğer Hidatik Kistine Bağlı Bilioplevral Fistül

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### Öz

Hidatik kist (HK) hastalığı Echinococcus tenyalarının larvalarının neden olduğu, fekal oral yolla bulaşan paraziter bir enfeksiyondur. İnsan vücudunda en sık karaciğerde paraziter enfeksiyona neden olmaktadır. İkinci sıklıkta yerleştikleri organ ise akciğerlerdir. Karaciğer HK'e bağlı Bilioplevral fistül (BPF) nadir görülen bir durumdur. Hastadaki plevral efüzyonun yeşil renkte ve Plevra sıvısı/serum bilirubin oranının >1,0 üzerinde olması biliotoraksı desteklemektedir. Tedavide biliyer drenaj ve diyafragma tamiri yapılır. 53 yaşında bayan hasta. Karın ağrısı şikayeti ve halsizlik şikayetleri ile hastanemize başvurdu. 8 yıl önce karaciğer HK'i nedeniyle opere edilmişti. Yapılan tetkikler sonucunda bilioplevral fistül(BPF) tespit edildi. BPF sonucunda pnömotoraks ve biliotoraks gelişen hastaya drenaj ve cerrahi tedavi uygulandı.

**Anahtar Kelimeler:** Ekinokok, bilioplevral fistül, karaciğer hidatik kisti

### Abstract

Hydatid cyst (HC) disease is a fecal orally transmitted parasitic infection caused by the larvae of Echinococcus tapeworms. In the human body, they cause parasitic infections most commonly in the liver. The second most common organ is the lungs. Biliopleural fistula (BPF) due to liver HC is a rare condition. Green pleural effusion and the pleural fluid/serum bilirubin ratio being >1.0 are supportive indicators of biliothorax. Treatment involves biliary drainage and diaphragm repair. A 53-year-old female patient. She consulted our hospital with complaints of abdominal pain and asthenia. She had undergone an operation for liver HC 8 years ago. Biliopleural fistula (BPF) was detected after examinations. Drainage and surgical treatment were performed on the patient who developed pneumothorax and biliothorax as a result of BPF.

**Key words:** Echinococcus, biliopleural fistula, hepatic hydatid cyst

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## INTRODUCTION

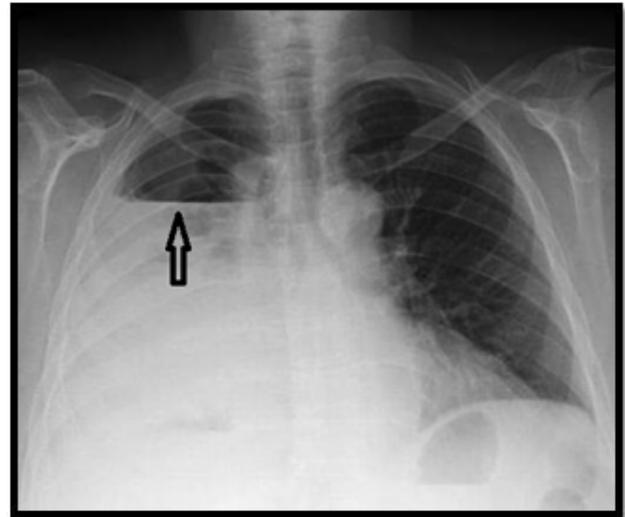
Hydatid cyst (HC) disease is a parasitic infection caused by the larvae of *Echinococcus* tapeworms. It is transmitted to humans by the fecal-oral route (1). HC disease was first reported by Thebesius in the 17th century and stated to be caused by the dogs of Icelandic fishermen (2,3). It is a common disease in countries focusing on husbandry such as the Mediterranean, Middle Eastern, and South American countries (4). There are 4 forms of *Echinococcus* that can cause disease in humans. Mostly, *Echinococcus granulosus* causes parasitic infections in humans (4,5). To complete their life cycle, they need 2 different hosts, namely the main host and middle host. Animals such as wolves, dogs, and foxes are the main hosts, and the cysts in the intestines of these animals can reach their adult form. In middle hosts such as humans, sheep, and cattle, the larva form of the cyst causes HC disease (5,6).

A significant proportion of embryos entering the human body cause parasitic infection most commonly in the liver since they get stuck in the liver sinusoids acting as a filter. Embryos smaller than 0.3 mm in diameter can pass through liver sinusoids. These embryos arrive at the right valve via the hepatic vein and inferior vena cava (IVC) and reach the lungs, the second most commonly infected organ (6). Bilioleural fistula (BPF) is a rare condition. Generally, liver hydatid cyst develops as a secondary complication to cholelithiasis, choledocholithiasis, malignancy, and surgery (7).

## CASE

A 53-year-old female patient. She consulted our hospital with complaints of abdominal pain and asthenia. She had undergone an operation for liver HC 8 years ago. Liver enzymes (SGPT; 53,4U/L,GGT;124 U/L)were high, Crp;73,28 mg/l and the Indirect Hemagglutination Test (IHA) was positive. She was admitted to our hospital with a prediagnosis of colodecolythisis, after 'biliary sludge' was detected in the biliary tracts in the abdominal ultrasonography. The patient underwent endoscopic retrograde cholangiopancreatography (ERCP), and the cyst membrane was detected in the biliary tracts, and the membrane was removed by ERCP.

The patient, who found to be developed pneumonia and pleural effusion symptoms during follow-ups, underwent pneumonia treatment. The patient had chest pain, cough, and shortness of breath. There were rales during inspiration on lung auscultation.

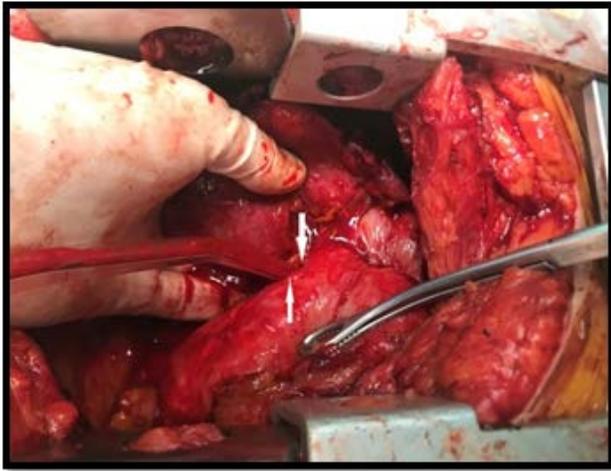


**Figure 1.** On the patient's posterior-anterior radiograph; pneumothorax line and air-fluid level

Pneumothorax was detected in the patient whose breathing is also deteriorated (Figure 1). The patient underwent closed underwater drainage and chest tube treatment, and it was observed that the fluid drained from the thorax of the patient contained bile. Green pleural effusion and pleural fluid/serum bilirubin ratio  $>1.0$  were supportive for biliothorax. The patient was diagnosed with a bilioleural fistula. When the vital symptoms of the patient, whose general condition was impaired, became stable, she was taken into operation. The patient underwent right thoracotomy. It was observed that both the visceral and parietal pleura of the patient were thickened. It



**Figure 2.** There was a fistula opening into the pleura in the lateral lower lobe of the lung and bile fluid was coming from this area.



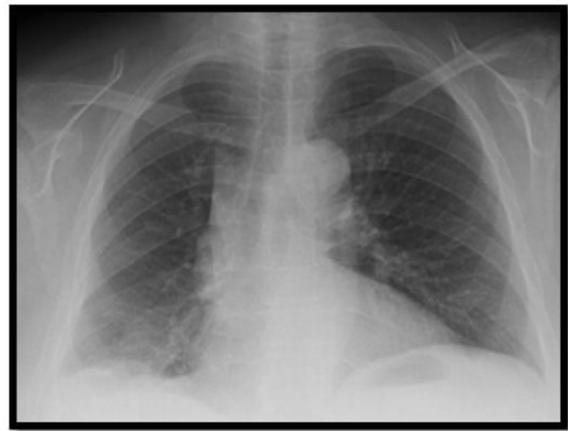
**Figure 3.** In the diaphragmatic dome, another fistula opening bile fluid was observed.

was found that the patient developed entrapped lung. It was observed that there was a fistula opening to the pleura in the lateral of the lower lobe of the lung and bile fluid was coming from this region (Figure 2).

The thickened visceral pleura of the patient was peeled off. The lungs were expanded. In the diaphragmatic dome, another fistula opening bile fluid was observed (Figure 3). The cystic membrane, which can be seen from the fistula opening in the diaphragm, was removed. Fistula in the diaphragm and lower lobe were repaired with primary sutures. Lung expansion was provided (Figure 4).



**Figure 4.** Lung expansion was provided



**Figure 5.** Posteroanterior chest radiography 2 months after

The patient, whose drainage was found to be stopped during postoperative follow-ups, was discharged after her general condition was improved. The general condition of the patient was good in the 2-month follow-up after discharge (Figure 5).

#### **Diagnosis**

Radiological and serological tests are used in the diagnosis of HC. Peripheral blood eosinophilia, increased leukocytosis, and sedimentation rate can be seen in ruptured cysts. However, the symptoms are nonspecific. The diagnostic value of Casoni and Weinberg tests - different serological tests - is around 52% (8). The positivity rate of the Indirect Hemagglutination Test (IHA) method indicating the presence of *Echinococcus granulosus* antibodies, was found to be 78.3% (9). The result of the IHA test was also positive in the case of our patient.

Serological tests were found to be more sensitive in liver cysts. This rate varies between 85% and 98% in liver cysts and 50-60% in pulmonary cysts (6). Our patient had a primer liver hydatid cyst. Since our patient also had symptoms of pneumonia, leukocytosis and increased sedimentation were evaluated as nonspecific symptoms. There are publications in the literature reporting that over 90% of the diagnoses can be made with posteroanterior chest PA radiography and thoracic computerized tomography (CT) (8). Ultrasonography can also be used for liver HCs (5). In our patient, the perforating of the cyst and the occurrence of biliopleural fistula caused pleural effusion and pneumothorax. ERCP is the most used method for the diagnosis of BPF (7). We also used ERCP for our patient. Cyst membranes were found in ERCP, and they were removed.

The dark green color of the pleural effusion and the pleural fluid/serum bilirubin ratio being  $>1.0$  support the diagnosis of biliopleural fistula (10). The pleural effusion in our patient was dark green and the pleural fluid/serum bilirubin ratio was above 1.0.

### **Treatment**

The main treatment of lung HC is surgery. Surgical treatment is recommended as soon as possible to prevent the risk of HC rupture(11). However, medical treatment is recommended for patients with concomitant diseases that cannot be surgically treated and patients with too many cysts that cannot be surgically removed. Unfortunately, oral treatment with albendazole or mebendazole has not been successful in this case (12).

Different tissue features of the liver and lungs may lead to different development of HC disease. Percutaneous treatment used for the livers is not suitable for the lungs (13). While the liver has a solid structure, the lung has a soft structure and contains air. Percutaneous treatment in the lung may cause infection with the communication from a residual bronchogenic cyst (13).

There is no standard surgical technique for the treatment of BPF due to HC. Biliary fistula is still a common complication after surgery. Treatment is basically based on the drainage of the pleural biliary fluid and surgically closing the fistula. In our patient, we first used a chest tube to treat pneumothorax and pleural effusion. When the general condition of the patient has improved, we peeled the visceral pleura thickened by right thoracotomy and closed the fistula openings in the lung parenchyma and diaphragm. ERCP is used both as a diagnosis and treatment method in biliopleural fistula (14). In our patient, cysts were found after ERCP and they were removed. Unfortunately, the fistula could not be closed. After pneumothorax symptom was also detected in the patient, firstly a chest tube was inserted into the patient, and drainage procedure was performed. When the general condition of the patient improved, the patient underwent right thoracotomy.

### **DISCUSSION**

HC causes disease most commonly in the liver (70%) and secondly in the lung 20% (6). In the literature, the coexistence rate of lung HC and liver HC is reported at 10-20% (11). HCs may rupture due to tension due to growth in size, trauma, or surgery. Rupture can be intraperitoneal or intrapleural. They can also cause damage to the biliary tracts, causing

rupture of the intrabiliary areas. Different rates of biliary fistula are reported in the literature 2.5-26.4% (10,15). Intrathoracic spread is at 0.6-16%. The addition of intrapleural negative pressure to the chemical effect of bile content is one of the factors leading to the occurrence of biliopleural fistula(7). It has been reported that the most common cause of BPF is tumors with a rate of 32.3% (2,6).

The green color of the pleural fluid and the ratio of pleural fluid bilirubin to serum bilirubin being greater than 1 are strong evidence of biliothorax (16). In thoracoabdominal traumas, biliary calculus perforation and pleural fluid (Biliothorax) in cholecystitis may occur, aside from liver hydatid cysts (16). Biliary fistula may develop from the biliary tracts to the pleura, after bile duct obstruction, or after cholecystectomy. Treatment involves biliary drainage and diaphragm repair.

### **Outcome And Follow-Up**

Liver HC is one of the rare causes of BPF. In the examinations of our patient, dark green pleural effusion and the pleural fluid/serum bilirubin ratio being  $>1.0$  were evaluated in favor of BPF. BPF treatments are biliary drainage and fistula repair. We first performed drainage with a chest tube for our patient. Then, by applying right thoracotomy, the fistula in the parenchyma and diaphragm was repaired, and the thickened visceral pleura that prevented lung expansion was peeled off. In the postoperative period, rapid improvement in her general condition was observed. The general condition of our patient is very good in the 2 months after the operation.

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