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Evaluation of Psychological Symptoms and Quality of Life in Patients with Early-Stage Mycosis Fungoides: A Case-Control Study

Erken Evre Mikozis Fungoides Hastalarında Psikolojik Belirtiler ve Yaşam Kalitesinin Değerlendirilmesi: Bir Vaka-Kontrol Çalışması

[1]Esra Ağaoğlu, [2] Hanife Merve Akça, [1]Niyazi Kürşat Çayır, [1]Hilal Kaya Erdoğan, [1]Ersoy Acer

[1]Eskisehir Osmangazi University Faculty of Medicine, Department of Dermatology, Eskisehir, Türkiye
[2]Karamanoğlu Mehmetbey University Faculty of Medicine, Department of Dermatology, Karaman, Türkiye

ORCID ID of the authors
EA. 0000-0001-8985-6224
HMA. 0000-0001-8280-7470
NKÇ. 0009-0004-0486-3679
HKE. 0000-0002-8172-1920
EA. 0000-0002-6041-6636

Correspondence / Sorumlu yazar:
Esra AĞAOĞLU

Eskisehir Osmangazi University Faculty of Medicine, Department of Dermatology, Eskisehir, Türkiye

e-mail: esraeagaoglu@gmail.com

Abstract: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma. This study was designed to measure psychological symptoms and health-related quality of life in patients with early-stage MF and compare the results with controls. Forty patients with early-stage MF and 40 age- and gender-matched healthy controls were included in the study. The sociodemographic characteristics of all participants were recorded and Depression, Anxiety and Stress Scale-21 (DASS-21) was administered to measure depression, anxiety and stress levels. Additionally, Skindex-29 was applied to assess the quality of life in MF patients. No significant difference was detected between patient and control groups of MF regarding DASS-21 subscales scores and the total scores. Both symptom and emotion subscale scores of Skindex-29 were found to be statistically higher in female MF patients. Older MF patients had worse symptoms and functional impairment according to Skindex-29. The DASS-21 total scores were positively correlated with all Skindex-29 subscale scores in MF patients. In conclusion, this study demonstrated that quality of life in early-stage MF may be negatively affected in elderly and female patients. Health-related quality of life was more affected in patients with increased levels of depression, anxiety and stress. The quality of life of MF patients can be increased by improving their psychological health.
Keywords: Mycosis fungoides, depression, anxiety, stress, quality of life

Ethics Committee Approval: This study was approved by the Ethics Committee of the Eskisehir Osmangazi University (Decision no: 51, Date: 03.10.2024).

Informed Consent: The authors declared that informed consent form was signed by the patient.

Authorship Contributions: All authors contributed equally to the study.

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Özet: Mikozis fungoides (MF) en sık görülen kutanöz T hücreli lenfoma türüdür. Bu çalışma erken evre MF hastalarında psikolojik belirtiler ve sağlıkla ilişkili yaşam kalitesini ölçmek ve sonuçları kontrollerle karşılaştırmak amacıyla tasarlanmıştır. Çalışmaya erken evre MF tanılı 40 hasta ve yaş ve cinsiyete uygun 40 sağlıklı kontrol dahil edildi. Tüm katılımcıların sosyodemografik özellikleri kaydedildi ve depresyon, anksiyete ve stres düzeylerini ölçmek için Depresyon, Anksiyete ve Stres Ölçeği-21 (DASÖ-21) uygulandı. Ayrıca, MF hastalarında yaşam kalitesini değerlendirmek için Skindex-29 uygulandı. MF'li hasta ve kontrol grubu arasında DASS-21 alt ölçek puanları ve toplam puanlar açısından anlamlı bir fark saptanmadı. Skindex-29'un semptom ve duygu alt ölçek puanları kadın MF hastalarında istatistiksel olarak daha yüksek bulundu. Skindex-29'a göre ileri yaş MF hastalarının daha kötü semptomları ve işlevsel bozuklukları bulunmaktaydı. DASS-21 ölçeği toplam puanları MF hastalarında tüm Skindex-29 alt ölçek puanlarıyla pozitif korelasyon gösterdi. Sonuç olarak erken evre MF'te yaşam kalitesi ileri yaş ve kadın hastalarda olumsuz olarak etkilenebilmektedir. Depresyon, anksiyete ve stres düzeyleri yüksek hastalarda sağlıkla ilişkili yaşam kalitesinin daha fazla etkilendiği görüldü. MF hastalarının psikolojik sağlıklarının iyileştirilmesiyle yaşam kaliteleri artırılabilir.
Anahtar Kelimeler: Mikozis fungoides, depresyon, anksiyete, stres, yaşam kalitesi

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1. Introduction

Mycosis fungoides (MF) is a mature primary T-cell lymphoma of the skin. It is characterized by the monoclonal proliferation of CD4+ T cells located in the skin. As the most common form of primary cutaneous lymphomas, MF constitutes approximately 60% of all primary non-Hodgkin lymphoma of the skin (1). MF is generally seen in older patients with median age at diagnosis between 55 and 60 years old and affecting more men than women (1.6–2.0:1). The majority of MF patients are diagnosed with early-stage disease. In the early stage of the disease, skin lesions typically appear as erythematous and atrophic patches located in non-sun-exposed areas of the body, often accompanied by itching with variable concomitant ulceration and alopecia (2, 3).

The staging of the MF is based on the TNMB (tumor-node-metastasis-blood) classification revised by the International Society of Cutaneous Lymphoma (ISCL)/European Organization for Research and Treatment of Cancer (EORTC). According to this classification, stage IA, IB or IIA is considered early-stage MF and most patients are diagnosed at this stage (4). Clinically, MF progresses through four stages: patch, plaque, tumor, and erythroderma. The most important prognostic factors in MF include the patient's age, the type and extent of skin involvement, the stage of the disease, the presence of extracutaneous involvement, and the detection of pathological cells in peripheral blood. Skin-directed therapies including topical corticosteroids, topical retinoids, phototherapy and localized radiotherapy are recommended in the treatment of early-stage MF (2, 3, 5).

Beyond the burden of the disease itself, the chronic, recurrent course of disease significantly impact negatively the patients' quality of life. Even in patients with an early-stage of disease, frequent hospital visits, diagnostic procedures, and the possibility of treatment-related side effects may cause anxiety in patients. Additionally, the psychosocial effects of fatigue and sleep disorders may increase the anxiety level of patients and lead to depressive mood disorders (6-8). Considering the effects of psychosocial health of the disease, in this study we aimed to evaluate the depression, anxiety and stress levels and quality of life in early-stage MF.

2. Materials and Methods

Study Population and Recruitment

We enrolled 40 early-stage MF patients and 40 healthy controls aged between 18-80 years. The study protocol was approved by Eskisehir Osmangazi University Ethics Committee. All individuals signed the informed consent form. We confirmed the diagnoses of all MF patients by histopathologically. Exclusion criteria included the use of psychotropic medication concurrently or within the previous 6 months. Sociodemographic data of the volunteers were recorded. In MF patients, the age of disease onset, duration of disease, presence of concomitant systemic or skin disease, stage of the disease, pathological lymph node involvement and current treatments were recorded by a dermatologist. The control group consisted of those who applied to our outpatient clinic with diagnoses such as melanocytic nevus or verruca vulgaris and hospital staff who did not have any psychodermatological disease.

Questionnaires

We evaluated the participants' status of depression, anxiety and stress with Depression Anxiety Stress Scale-21 (DASS-21) which is developed by Lovibond et al. in 1995 (9). DASS-21 consisted of three subscales each containing seven items scored between 0 and 3. The 21 items of the scale were evaluated on a 4-point Likert Scale (0 = Not at all, 1 = applied to me to some degree or some of the time, 2 = applied to me to a considerable degree or a good part of the time, 3 = applied to me very much or most of the time). The validity and reliability of the Turkish version of the DASS-21 was conducted by Sarıcam (10).

MF patients' quality of life was measured by Skindex-29 which is developed by Chren et al (11). This instrument is a self-administered 29-item questionnaire that explores 3 specific aspects of quality of life: effects of skin disease on functioning, emotions and physical symptoms. The answers of the scale are evaluated by converting them to a linear scale, with the "never" option being "0" and the "always" option being "100". Higher scores indicate a greater effect of skin disease on quality of life. The Turkish version of Skindex-29 was established successfully with validity and reliability (12).

Statistical Analysis

The data analyses were performed with SPSS 21.0 Software Package Program Inc., Chicago. Considering the data numbers in the evaluated groups, the relevant data were examined in terms of compliance with normal distribution using one of the Kolmogorov-Smirnov or Shapiro-Wilk tests. Kruskal Wallis H test and Mann Whitney U test were used for data that did not comply with normal distribution. One-Way ANOVA test was used for data that complied with normal distribution, post-hoc Tukey test and Independent-Samples T test were used for comparisons between groups. Since all data evaluated for correlation did not comply with normal distribution, Spearman correlation analysis was used in all correlation evaluations performed in the study. Chi-square test was used for evaluation of categorical data. In all analyzes, $p<0.05$ was considered statistically significant.

3. Results

Of the MF patients, 21 (52.5%) were male and 19 (47.5%) were female. Of the control group, 20 (50.0%) were male and 20 (50.0%) were female. Mean age was 55.32 ± 13.64 in MF group and was 50.72 ± 12.53 in control group. MF patients and controls were similar by distribution of gender, age and marital status ($p>0.05$). The mean disease duration of MF patients was 11.28 ± 14.67 months (Table-1). Thirty-one (77.5%) of the MF patients were stage IA, 5 (12.5%) were stage IB, and 4 (10.0%) were stage IIA. Fifteen (37.5%) of our patients were receiving topical steroids, 9 (22.5%) were receiving topical steroids and acitretin, 8 (20.0%) were receiving topical steroids and narrow-band ultraviolet B phototherapy, and 3 (7.5%) were receiving topical steroids and topical bexarotene. Reactive lymph node involvement was detected in 3 (7.5%) of the MF patients and none of the patients had pathologic lymph node involvement. There were no significant differences between patient and control groups of DASS-21 subscales scores and the total scores ($p> 0.05$) (Table-2).

Table 1. Characteristics in MF patients and control groups

Characteristics	Patient group	Control group	p
Sex			
Male	21 (52.5%)	20 (50.0%)	0.823
Female	19 (47.5%)	20 (50.0%)	
Age			
Mean±SD	55.32±13.64	50.72±12.53	0.120
Range	33-77	26-73	
Marital status			
Married	30 (75.0%)	29 (72.5%)	0.799
Single	10 (25.0%)	11 (27.5%)	
Mean disease duration (month)	11.28±14.67		

Table 2. Comparison of DASS-21 scale scores in MF and control groups

Characteristics	Patient group		Control group		P
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)	
DASS-21-Depression	4.68±0.63	4.0 (0-18)	4.20±1.92	4.0 (0-8)	
DASS-21-Anxiety	4.28±0.56	3.5 (0-16)	4.15±2.04	4.0 (0-8)	p> 0.05
DASS-21-Stress	4.95±0.61	4.0 (0-18)	4.48±1.85	5.0 (0-8)	
DASS-21-Total	13.9±1.72	13.0 (0-52)	12.83 ± 0.76	14.0 (1-19)	

The mean total Skindex-29 questionnaire score for the MF patients was 23.62 ± 15.40 (median=20.68). The mean symptom subscale of Skindex-29 was 33.92 ± 17.04, while emotion subscale was 25.43 ± 18.99 and functioning subscale was 16.09 ± 15.37.

When the correlation between Skindex-29 subscales according to gender was examined, the symptom and emotion subscale scores were found to be statistically higher in female MF patients ($p \leq 0.05$). There were no significant differences between the stage of the disease and the Skindex-29 subscales ($p> 0.05$) (Table-3).

Table 3: Correlation of the Skindex-29 subscale scores between gender and stage of the disease

Skindex-29 domains	Sex		p	Stage			p
	Female	Male		1A	1B	2A	
Symptom	41.9 ± 4.1 42.8 (0-67)	26.7±2.7 32.1 (7.1-46.4)	**0.03**	31.3±2.9 32.1 (0-67.8)	44.2±6.3 39.2 (32.1-64.2)	41.0±11.1 41.0 (14.2-67.8)	> 0.05
Emotion	34.21 ± 5.29 32.5 (2.5-90.0)	17.50 ± 2.01 17.50 (0-32.5)	**0.006**	24.83±3.64 22.5 (0-90.0)	22.0±5.14 20.0 (10.0-40.0)	34.3±8.1 37.5 (12.5-50.0)	> 0.05
Functioning	20.50 ± 4.44 14.5 (0-66.6)	12.10 ± 1.91 8.33 (0-31.2)	0.27	14.9±2.8 12.5 (0.0-66.6)	18.3±4.85 16.6 (8.3-33.3)	22.3±7.6 21.8 (4.1-41.6)	> 0.05

**: Number are displayed as mean± standard deviation and median (range).*

Significant positive correlation was detected between age and symptoms and functioning subscale scores ($p \leq 0.05$). Additionally, DASS-21 total scores were positively correlated with all Skindex-29 subscale scores ($p \leq 0.05$) (Table-4).

Table 4. Correlation of Skindex-29 subscale scores between age, duration of disease and DASS-21 total scores in MF patients

Skindex-29 domains	Age	Duration of disease	DASS-21 score (total)
Symptoms	p=0.01*	p=0.227	p=0.000*
	r=0.404	r=0.160	r=0.546
Emotion	p=0.08	p=0.919	p=0.000*
	r=0.277	r=-0.017	r=0.658
Functioning	p=0.001*	p=0.360	p=0.000*
	r=0.486	r=0.149	r=0.558

**: Positive correlation between the variables.*

3. Discussion

MF is a chronic cutaneous T-cell lymphoma typically presents in its early stage. The disease can be difficult to diagnose in its earliest stages because it may mimic a number of benign skin disorders. Although MF is a disease with low risk of progression and a slowly progressing course, for which no effective cure is available. MF is a disease that is difficult to differentiate and negatively affects the quality of life of patients. Patients were almost always affected by a wide range of symptoms such as redness, scaling and pruritus due to the disease (5, 7).

Psychological morbidity is common in patients with hematologic malignancies and could negatively influence patients' life. Frequent hospital visits, diagnostic procedures, treatment-related side effects, and fear of death may cause psychiatric conditions such as depression and anxiety in MF patients (6, 7). In our study, we evaluated the DASS-21 scores of MF patients and compared it with a group of healthy controls. To the best of our knowledge, there is no study evaluated the depression, anxiety and stress status in MF patients using the DASS-21 scale. In our study, the mean depression, anxiety and stress subscales of DASS-21 were 4.28, 4.28 and 4.95, respectively. However, we found no significant difference in DASS-21 scores between MF patients and controls. Several studies on chronic inflammatory diseases such as acne and psoriasis have found higher DASS-21 scores than our study (13-15). This may be due to the fact that most of our MF patients were in the early stages which has a good response to skin-directed therapies. In addition, acne and psoriasis can affect visible areas such as

the face, which can cause further deterioration in the psychological status of patients.

In our study, health-related quality of life was evaluated using the Skindex-29 questionnaire in MF patients. In the literature, there are several studies measured the impact of skin disease on health-related quality of life using the Skindex-29 questionnaire (16-19), although it does not comprise cancer-spesific items. Sampogna et al. reported a study comparing the quality of life in patients with cutaneous lymphomas and other dermatological diseases. This study showed that patients with even more severe stages of cutaneous lymphoma reported a similar quality of life impairment to psoriasis patients. Additionally, they revealed that emotional functioning was similar to the patients with vitiligo. They concluded that this may be related to the visible aspect of the psoriasis and vitiligo diseases (16).

The median global Skindex-29 questionnaire score of our study population was 20.68. When the Skindex-29 subscale scores in our study were compared with the literature (20, 21), the symptom subscale scores were found to be similar, while the emotion and functioning subscale scores were found to be lower than these studies. Female MF patients had significantly worse symptom and emotion Skindex-29 subscale scores compared to male patients. Recently, a large cohort study also demonstrated that the greatest impact on symptoms and emotions subscales of the Skindex-29 in patients with cutaneous T cell lymphoma (22). Molloy et al. reported a study for identifying the factors associated with poorer health-related quality of life in a large study population of 236 newly diagnosed MF patients. Similarly, they found that as measured by Skindex-29, female patients with MF have a significantly worse symptom and emotion subscale scores compared to male patients (19). These gender differences regarding health-related quality of life in patients with cutaneous lymphoma have also been demonstrated (16, 18). Eder et al. evaluated the illness perception in primary cutaneous T-cell lymphomas and they showed that women perceive the disease as more chronic than men (18). Sampogna et al. showed that a worse quality of life was observed in female patients for all the subscales of Skindex-29 in patients with cutaneous lymphomas (16). It has been reported that quality of life has been more impaired in female patients with inflammatory skin diseases such as psoriasis, atopic dermatitis and vitiligo, as well as in non-Hodgkin lymphoma compared to male patients (23-26). This may be related to the women tend to be more emotionally affected by their disease than men.

It is expected that stage of MF negatively correlated the patients' quality of life. Previous studies showed that quality of life was more affected in patients with advanced-stage MF (16, 22, 27, 28). It is also reported that patients with advanced-stage disease have more impairment in general health status, emotional well-being, fatigue and insomnia (16). However, Holahan et al. used Skindex-16 for evaluating the health-related quality of life and did not find a direct relationship between stage and quality of life. They suggested that this may be due to the earlier stage of disease of their patients (29). Similarly, we did not find a positive correlation between stage of the disease and Skindex-29 subscale scores. This may be because of our study included only patients with early-stage disease, and 77.5% of them were in stage 1A, where there were a limited number of lesions.

In our study, we also revealed a positive correlation between age and symptoms and functioning subscale scores in early-stage MF patients. Several studies also showed that younger patients with non-Hodgkin lymphoma have higher quality of life (30-32). Although most of our patients were at stage IA, elderly patients may have a reduced ability to cope with chronic skin diseases or manage symptoms. We also found that DASS-21 total scores were positively correlated with all Skindex-29 subscale scores in our MF patients. This indicates that psychological conditions such as depression, anxiety and stress that develop due to even the early-stage MF may lead to the worsening of the symptoms, emotions or functioning.

The limitations of our study are its a single-center design and the small sample size of MF patients including only Turkish population. Studying the quality of life and psychological health throughout the country may provide different insights into evaluation of patients.

In conclusion, this study demonstrated that female MF patients had more symptoms and emotional impairment related to disease. Additionally, elderly MF patients had more cutaneous symptoms and functional deterioration. Even in the early stages of MF, health related quality of life was more affected in patients with increased levels of depression, anxiety and stress. By improving the psychological health of MF patients, their quality of life can be

better. We are of the opinion that further prospective studies are needed to elucidate our results.

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