HİTİT MEDICAL JOURNAL
HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

e-ISSN: 2687-4717 Cilt|Volume: 6 • Sayı|Issue: 3 - Ekim|October 2024

Investigation of Possible Predictive Factors, Clinical Characteristics, and Treatment in Vascular Behçet's Disease: Real-Life Data from a Single Center

Vasküler Behçet Hastalığında Olası Prediktif Faktörler, Klinik Karakteristikler ve Medikal Tedavinin Değerlendirilmesi: Tek Merkezden Gerçek Yaşam Verileri

Abdulvahap Kahveci[1] | Zeycan Kübra Cevval[2]

[1]Kastamonu Training and Research Hospital, Department of Rheumatology, Kastamonu, Türkiye.
[2]Kastamonu Training and Research Hospital, Department of Radiology, Kastamonu, Türkiye.

Sorumlu Yazar | Correspondence Author
Abdulvahap Kahveci
abdulvahap_kahveci@hotmail.com
Address for Correspondence: Kuzeykent District, 57. Alay Street, Cankat Street, No: 4, Kastamonu, Türkiye.

Makale Bilgisi | Article Information
Makale Türü | Article Type: Araştırma Makalesi | Research Article
Doi: https://doi.org/10.52827/hititmedj.1442618
Geliş Tarihi | Received: 25.02.2024
Kabul Tarihi | Accepted: 15.06.2024
Yayım Tarihi | Published: 14.10.2024

Atıf | Cite As
Kahveci A, Cevval ZK. Investigation of Possible Predictive Factors, Clinical Characteristics, and Treatment in Vascular Behçet's Disease: Real-Life Data from a Single Center. Hitit Medical Journal 2024;6(3): 281-288.https://doi.org/10.52827/hititmedj.1442618

Hakem Değerlendirmesi: Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
Etik Beyanı: Kastamonu Üniversitesi Klinik Araştırmalar Etik Kurulu' ndan çalışma için etik onay alınmıştır. (Tarih: 6/12/23; protokol numarası: 2023-KAEK-149).
İntihal Kontrolleri: Evet (iThenticate)
Çıkar Çatışması: Yazarlar herhangi bir çıkar çatışması olmadığını beyan etmişlerdir.
Şikayetler: hmj@hitit.edu.tr
Katkı Beyanı: Fikir/Hipotez: AK, ZKC Tasarım: AK, ZKC Veri Toplama/Veri İşleme: AK, ZKC Veri Analizi: AK, ZKC Makalenin Hazırlanması: AK, ZKC.
Hasta Onamı: Hasta onamına gerek yoktur.
Finansal Destek: Bu çalışma ile ilgili herhangi bir finansal kaynaktan yararlanılmamıştır.

Peer Review: Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
Ethical Statement: The study was granted approval by the Kastamonu University, Faculty of Medicine, Ethics Committee of Clinical Research (date: 6/12/23; protocol number: 2023-KAEK-149).
Plagiarism Check: Yes (iThenticate)
Conflict of Interest: The authors declared that, there are no conflicts of interest.
Complaints: hmj@hitit.edu.tr
Authorship Contribution: Idea/Hypothesis: AK, ZKC. Design: AK, ZKC. Data Collection/Data Processing: AK, ZKC. Data Analysis: AK, ZKC. Manuscript Preparation: AK, ZKC.
Informed Consent: Not applicable.
Financial Disclosure: There are no financial funds for this article.

Investigation of Possible Predictive Factors, Clinical Characteristics, and Treatment in Vascular Behçet's Disease: Real-Life Data from a Single Center

ABSTRACT

Objective: The aim of this study was to investigate the phenotypes, predictive factors, and treatment approach of Behçet's patients with vascular involvement.

Material and Method: This retrospective study analyzed 123 patients with Behçet's disease, 28 of whom had vascular involvement, and were followed up in our center. The study presented the vascular involvement patterns of the patients along with their clinical characteristics and comorbid conditions. The drugs usage by the patients were analyzed based on the first line and current medications, duration of medical therapy, and drug retention rate.

Results: In Behçet's patients with vascular involvement, the male sex ratio was statistically higher compared to those without vascular involvement (60.7% vs 37.9%; OR=2.82 (1.17-6.77); *p=0.018*). The frequencies of Behçet's clinical manifestations, smoking, and comorbidities were similar in both groups. The most common subtype of vascular Behçet's is deep vein thrombosis (18; 64.2%), followed by superficial thrombophlebitis (5; 17.8%), neurovascular involvement (5; 17.8%), cardio-aortic (2; 7.1%) and pulmonary arterial (2; 7.1%). Azathioprine, glucocorticoids, and cyclophosphamide are the most preferred immunosuppressives in vasculo-Behçet's. Anticoagulant therapy was initiated in 67.8% (19; 28) of the patients at the first vascular event.

Conclusion: The study presented that male gender predicts vascular involvement in Behçet's disease, with deep vein thrombosis being the most common vascular subtype. Although immunosuppressive drugs represent the cornerstone of treatment for vasculo-Behçet's disease, most patients had also received anticoagulant therapy following the initial attack.

Keywords: Anticoagulant, Behçet's Disease, drug retention, immunosuppressive, real-world data, vascular involvement.

ÖZET

Amaç: Bu çalışmanın amacı vasküler tutulumu olan Behçet hastalarının tutulum paternlerini, prediktif faktörleri ve tedavi seçimlerini ortaya koymaktır.

Gereç ve Yöntem: Bu çalışmaya merkezimizde takipli 28'i vasküler tutulumlu olan 123 Behçet hastası retrospektif olarak dahil edildi. Hastaların vasküler tutulum paternleri diğer klinik karakteristikleri ve komorbid durumları ile sunuldu. Hastaların kullandıkları ilaçlar ilk başlanılan ajan, mevcut kullanılan ajan, kullanım süresi ve ilaçta kalım değişkenlerine göre analiz edildi.

Bulgular: Vasküler tutulumu olan Behçet hastalarında erkek cinsiyet oranı, vasküler tutulum olmayanlara göre istatistiksel olarak yüksekti (%60,7 vs. %37,9; OR=2,82 (1,17-6,77); *p=0,018*). Her iki grupta Behçet klinik tutulumları, sigara içimi ve komorbidite frekansları benzer bulundu. En sık görülen vasküler Behçet subtipi derin ven trombüsü (18; %64,2) olup onu sırasıyla süperfisyal tromboflebit (5; %17,8), nörovasküler tutulum (5; %17,8), kardiyo-aortik (2; %7,1) ve pulmoner arteriyel tutulum (2; %7,1) izledi. Vasküler Behçet'te en sık tercih edilen immunsupresifler azatioprin, glukokortikoid, siklofosfamid olup antikoagülan tedavi hastaların %67,8 (19; 28)'inde ilk vasküler olayda başlanmıştı.

Sonuç: Bu çalışmada erkek cinsiyetin Behçet Hastalığı'na bağlı vasküler tutulumu predikte ettiği gösterildi. Derin ven trombüsü en sık görülen vasküler Behçet subtipiydi. Vaskülo-Behçet'te immunsupresif ilaçlar ana tedavi olmasına rağmen hastaların büyük bir kısmı ilk atak sonrası antikoagülan tedavi de almıştı.

Anahtar Sözcükler: Antikoagülan, Behçet Hastalığı, gerçek yaşam verisi, ilaçta kalım, immünsupresif, vasküler tutulum.

Introduction

Behçet's disease (BD) is a multisystemic autoinflammatory vasculitis that affects multiple organs, including the mucocutaneous, ocular, vascular, neurological, and intestinal systems (1). The disease is characterized by pan-vasculitis, which affects veins and arteries of all sizes (2). Vascular involvement is the leading cause of mortality in BD, with particularly high mortality rates observed in cases of pulmonary and inferior vena cava involvement (2).

The frequency of vascular involvement in BD has been reported to range between 7% and 40% in different studies (3,4). The most common type of major vascular involvement is deep vein thrombosis (2). Arterial involvement is characterized by thrombosis and aneurysms and is less common than venous involvement (5,6). Superficial thrombophlebitis is considered a form of vascular involvement but is excluded from the definition of major vascular involvement.

The treatment of Vascular BD involves the use of immunosuppressive drugs (5). According to European Alliance of Associations for Rheumatology (EULAR) treatment recommendations, the first-line agents used are glucocorticoids (GC), azathioprine (AZA), and cyclophosphamide, although the specific choice may vary depending on the type of involvement (7). In cases of resistance or contraindication to immunosuppressives, biological therapies such as anti-TNF may be employed (7). The available evidence on the use of anticoagulant therapy for vascular involvement in BD is insufficient (6-8).

Many studies, including EULAR recommendations, provide drug recommendations based on the involvement patterns in vascular BD (2,5,8). However, the duration of immunosuppressive treatment remains unclear. Several Behçet's clinics have shared their experiences on this subject in the literature (2,4,5,8-10). In this respect, this study aimed to present the predictive factors, clinical characteristics, and treatment approaches of Behçet's patients followed up in our clinic, especially the subtypes of vascular involvement.

Material and Methods

Study design and patients

This retrospective study analyzed 123 patients with BD who were followed up at the rheumatology clinic of Kastamonu Training and Research Hospital between November 2022 and December 2023 and met the International Study Group Criteria of Behçet's disease (11). The study retrospectively evaluated the clinical and demographic data obtained from the patients' outpatient clinic visits every three months. The demographic data of patients with BD includes information on patient age, gender, age at diagnosis, duration of vascular involvement, body mass index, smoking, and comorbidities such as diabetes mellitus, hypertension, renal failure, coronary artery disease, and asthma/bronchial disease. The study recorded various symptoms in Behçet's patients, including oral aphthae, genital ulcers, papulopustular lesions, erythema nodosum, pathergy test positivity, ocular involvement, musculoskeletal involvement, intestinal involvement, neurological involvement, and vascular involvement.

The presence of vascular involvement was determined in 123 patients using clinical and imaging methods such as ultrasonography, CT angiography, and MRI angiography. The study analyzed vascular involvement patterns, first-line and current medications, duration of medication for each drug, number of patients who discontinued and restarted the medication along with the reasons in 28 patients diagnosed with vasculo-Behçet's.

The International Study Group Criteria of BD comprises five headings: oral aphthae, genital ulcer, ophthalmic involvement, skin involvement, and positive pathergy test (11). BD is diagnosed in individuals who have at least two of the other clinical findings in addition to oral aphthae (11).

This study was approved by the Kastamonu University, Faculty of Medicine, Ethics Committee of Clinical Research (date: 6/12/23; protocol number: 2023-KAEK-149). The study followed the Declaration of Helsinki and good clinical practice guidelines.

Statistical analysis

All statistical analyses were performed using SPSS version 26 (IBM Corp, Armonk, NYC). The normal distribution of variables was analyzed using visual (histogram) and analytical methods (Kolmogorov/Smirnov test). Descriptive statistics were presented as mean ± standard deviation for continuous variables and as frequency (n) and percentage (%) for categorical variables. Student-T test was used to compare

normally distributed variables between the groups with and without vascular involvement. Chi-square/Fisher exact tests were used to compare nominal (CI) variables. The odds ratios (95% confidence interval) were used to express the association between clinical characteristics and vascular involvement. *p value less than 0.05* was considered statistically significant.

Results

A total of 123 patients with BD were included in this study, of whom 28 (22.7%) had vascular involvement and 95 (77.3%) did not have vascular involvement. The male gender was significantly more predominant in patients with vascular involvement than in those without (60.7% vs 37.9%; OR=2.82(1.17-6.77); *p=0.018*). The mean age, body mass index, and disease duration were similar in both groups (*p>0.05*). The average duration of vascular involvement in the group with vascular Behçet's was 16.2±9.2 years (Table I).

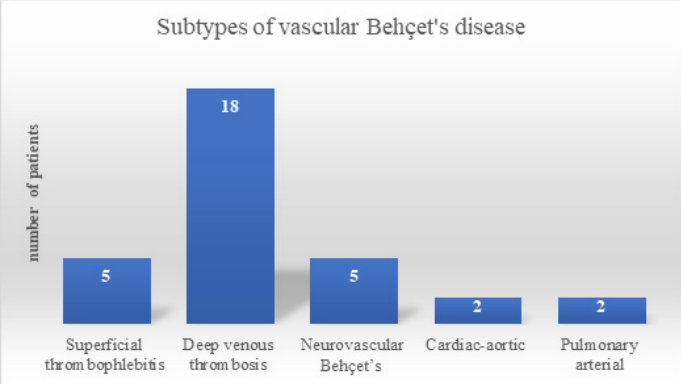

Figure I Classification of vascular involvement of Behçet's disease

The percentages of clinical involvement in Behçet's (oral aphthae, genital ulcer, papulopustular lesion, erythema nodosum, uveitis, arthralgia, intestinal and neuroparenchymal involvement) were similar in both groups, with and without vascular involvement (*p>0.05*). Additionally, both groups had similar rates of pathergy test positivity. The results of study revealed that variables other than gender had no statistically significant impact on vascular involvement (*p>0.05*) (Table I).

Table II shows the frequency of atherosclerosis-related risk factors for vascular involvement in Behçet's patients with and without vascular involvement. The results indicate that smoking was similar in both groups (46.4% vs 35.8%; *p=0.311*). Furthermore, the frequency of comorbidities, such as diabetes mellitus, hypertension, renal impairment, coronary artery disease, and pulmonary disease, was similar in both groups.

Table I Demographic and clinical characteristics of Behçet's patients with and without vascular involvement

	Vascular BD (n=28)	BD without vascular involvement (n=95)	*OR (95% CI)*	*P value*
Gender, male, n, %	17(60.7%)	36 (37.9%)	2.82(1.17-6.77)	***0.018***
Age, years, mean±SD	43.5±11.5	40.3±10.1		*0.195*
Disease duration, years, mean±SD	15.0±10.7	10.8±8.7		*0.135*
Duration of vascular involvement, years, mean±SD	16.2±9.2	-		
Body mass index, kg/m², mean±SD	27.1±3.9	26.3±5.2		*0.344*
Oral aphthous ulcer, n, %	28(100%)	94(98.9%)	0.98(0.96-1.01)	*0.587*
Genital ulcer, n, %	23(82.1%)	72(75.8%)	1.46(0.50-4.30)	*0.483*
Papulopustular lesion, n, %	19(67.8%)	60(63.2%)	1.23(0.50-3.01)	*0.650*
Erythema nodosum, n, %	18(64.3%)	52(54.7%)	1.55(0.64-3.71)	*0.322*
Pathergy positivity, n, %	20(71.4%)	69(72.6%)	0.94(0.37-2.40)	*0.901*
Uveitis, n, %	13(46.4%)	41(43.1%)	1.37(0.59-3.20)	*0.461*
Arthralgia/arthritis, n, %	19(67.8%)	65(68.4%)	0.97(0.39-2.40)	*0.955*
GIS involvement, n, %	1(3.5%)	1(1.1%)	3.48(0.21-57.51)	*0.356*
Neuroparenchyma involvement, n, %	3(10.7%)	2(2.1%)	5.58(0.88-35.23)	*0.077*

BD, Behçet's disease; SD, standard deviation; OR, odds ratio; CI, confidence interval; kg/m², kilogram/meter square, GIS, gastrointestinal system.

In the analysis of vascular Behçet's patients based on subtypes, deep vein thrombosis was found to be the most common (18; 64.2%). Superficial thrombophlebitis (5; 17.8%), neurovascular involvement (5; 17.8%), cardio-aortic (2; 7.1%), and pulmonary arterial (2; 7.1%) involvement were also detected, respectively (Figure I).

When examining the first line immunosuppressive treatments, glucocorticoids (27; 96.4%), azathioprine (18; 64.2%), and cyclophosphamide (9; 32.1%) were administered. Furthermore, 67.8% of patients received anticoagulant therapy upon diagnosis, despite the lack of conclusive evidence in vascular BD. Regarding to analysis of the current treatments of the patients, it was found that 17 (60.7%) patients used AZA and 7 (25%) patients used GC. Notably, no patients received cyclophosphamide. Furthermore, none of the patients were receiving anticoagulant treatment during their last treatment, while 4 patients were not receiving any form of treatment, including immunosuppressive and anticoagulant treatment (Figure II).

Table II Comorbidities in patients with of Behçet's patients with and without vascular involvement

	Vascular BD (n=28)	BD without vascular involvement (n=95)	OR (95% CI)	*P value*
Smoking, n, %	13(46.4%)	34(35.8%)	1.55(0.66-3.64)	*0.311*
Comorbidities, n, %				
-Diabetes mellitus	3(10.7%)	8(8.4%)	1.30(0.32-5.28)	*0.710*
-Hypertension	7(25.0%)	12(12.6%)	2.30(0.80-6.57)	*0.113*
-Renal failure	1(3.6%)	3(3.2%)	1.13(0.11-11.36)	*0.914*
-Coronary artery disease	3(10.7%)	4(4.2%)	2.73(0.57-13.00)	*0.194*
-Asthma/bronchial disease	2(7.1%)	3(3.2%)	2.35(0.37-14.87)	*0.350*

BD: Behçet's disease, OR, odds ratio; CI, confidence interval.

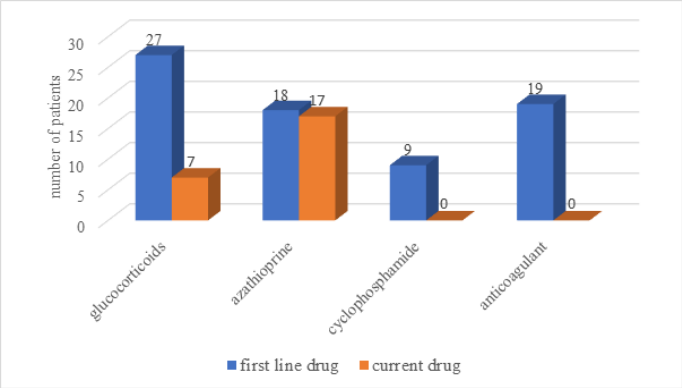

Figure II Drug retention rate of Behçet's disease, first line vs current treatment

The duration of use of immunosuppressive drugs was analyzed. AZA was used for the longest time with a mean of 11.2 (±5.8) years, followed by GC with 6.2 (±3.4) years, anti-TNF drugs with 3.5 (±1.2) years, and cyclophosphamide with 0.6 (±0.3) years (Table III). The mean duration of anticoagulant use was calculated to be 9.2 (±4.3) years.

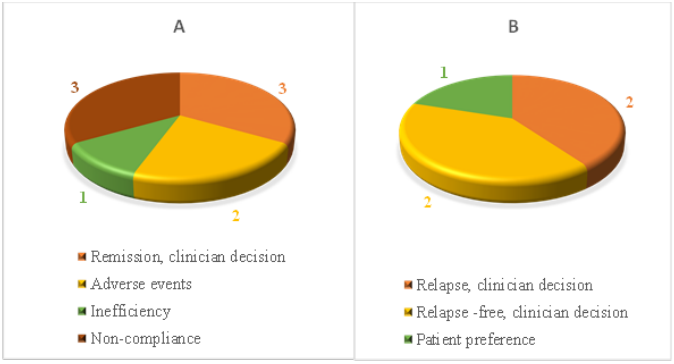

Figure III Reasons for discontinuation (A) and restarting (B) of immunosuppressive treatment

According to drug compliance of immunosuppressive treatment, it was found that treatment was discontinued for a period in 9 patients, with 5 of these patients subsequently restarting treatment. Figure III provides detailed information on the reasons for discontinuation and resumption of treatment.

Table III Duration of drug administration of vascular Behçet's patients

Drugs	Duration, year, mean (±SD)
Glucocorticoids	6.2 (±3.4)
Azathioprine	11.2 (±5.8)
Cyclophosphamide	0.6 (±0.3)
Anticoagulant	9.2 (±4.3)
anti-TNF	3.5 (±1.2)

TNF: Tumor necrosis factor.

Discussion

The study showed that the relative risk of male gender for vascular involvement was 2.82 (95% CI; 1.17 - 6.77; $p<0.05$) compared to female gender in patients with BD. This finding is consistent with previous studies on vascular Behçet's cohorts in the literature (4,10,12,13). Our study found that male gender was the only factor associated with vascular involvement. Other studies have shown a relationship between young age (4), erythema nodosum (12), ocular involvement

(12), neuroparenchymal involvement, and vascular involvement. Additionally, a retrospective study found a correlation between superficial thrombophlebitis and major vascular involvement (4).

No significant association was found between vascular BD and atherosclerosis-related factors, including smoking, diabetes mellitus, hypertension, and coronary artery disease, in our patients. The relationship between BD and atherosclerosis has been a controversial issue for years (6). A meta-analysis showed that subclinical atherosclerosis increased in patients with BD when evaluating coronary intima-media thickness (14). Furthermore, studies have demonstrated that patients with BD do not experience an increase in the frequency of coronary atherosclerosis, angina pectoris, or myocardial infarction (15,16).

The prevalence of vascular involvement in BD varies between ethnic groups. While it is less frequently observed (3-7%) in Far Eastern countries such as Japan, studies report a rate of around 40% in Türkiye (3,4). In this study, the prevalence of vascular BD was found to be 22.7% (28; 123). The most common presentation of vascular BD is deep vein thrombosis and superficial thrombophlebitis in the veins of the lower extremities (1,4,5,12,17). Neurovascular involvement characterized by thrombotic involvement in the venous sinuses of the brain is a vascular subtype of BD and is also classified as neuro-Behçet's. Consistent with the literature, this study found that deep vein thrombosis was the most common venous involvement, followed by superficial thrombophlebitis and sinus vein thrombosis. Although arterial lesions are less common in vascular BD (3-5%), they have a more severe course (2,4,5,10,12). Arterial involvement can be observed in all arterial structures, particularly the pulmonary artery. The study found arterial involvement in the pulmonary artery (2; 7.1%) and cardiac-aortic (2; 7.1%) vascular structures.

Immunosuppression is the primary treatment for vascular BD (2,5,7,8,18-20). The goal of immunosuppressive therapy is to reduce vessel wall inflammation and recanalization (2,5,7,8,19,20). In cases of venous involvement, treatment varies depending on the location and duration of the condition (acute/chronic). Glucocorticoids, azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil and biological agents (TNF inhibitors) are commonly used in practice (2,5,7,8,18-20). In this study, the combination of azathioprine and corticosteroids was the first choice for the patient group. Another combination, which is especially preferred in the clinic for major arterial aneurysm and/or thrombosis, is cyclophosphamide and corticosteroids.

The duration of immunosuppressive treatment for vasculo-Behçet's disease is a controversial issue. Studies have shown that patients receiving azathioprine for DVT had a 45% frequency of vascular relapse (21). In a larger cohort of vascular Behçet's patients, relapse was observed in 44.7% of patients with a mean follow-up of 24.5 months (22). In the same study, it was found that the median duration of immunosuppressive treatment after the first vascular event was 24 months. The study also showed that relapse occurred at a median of 34.5 months (22), indicating that early discontinuation of immunosuppressive treatment may increase the risk of relapse. In our patient group, the mean duration of azathioprine use was 11.2 (±5.8) years and steroid use was 6.2 (±3.4) years, which is a relatively long duration. During the last one-year follow-up period, two patients had to restart immunosuppressive treatment due to relapse.

Anticoagulant drugs are a controversial issue in treating vascular BD. According to EULAR recommendations, anticoagulant therapy can be used if there is no pulmonary artery aneurysm (7). However, there is no prospective study on the use of anticoagulants. A study conducted in Türkiye at multiple centers found no additional benefit in terms of relapse rates when anticoagulant therapy was used in conjunction with immunosuppressive therapy, compared to immunosuppressive therapy alone (19). However, a retrospective study conducted in another cohort showed a positive effect of anticoagulant therapy (20). In our patient group, 67.85% (19; 28) of vascular Behçet's patients were started on anticoagulant therapy at the first vascular event. The patients used anticoagulants for an average of 9.2 (±4.3) years. Currently, no patients are receiving anticoagulant therapy.

Inflammation plays a central role in the pathogenesis of vascular involvement in BD. In addition, endothelial dysfunction leading to a tendency to thrombosis,

increase in procoagulant factors and dysfunction of tPA are other subheadings of the pathogenesis (5). However, the use of anticoagulant drugs in treatment is contradictory. In the latest recommendations of EULAR, anticoagulant therapy is recommended for the prevention of postthrombophilic syndrome which may be a complication of deep vein thrombosis (7).

One of the limitations of this study is that due to the retrospective nature of the study, relapses were evaluated within the period of our own follow-up and old relapses were evaluated according to patient declaration and imaging method. Therefore, relapse-time relationship and relapse-treatment relationship (immunosuppressive and anticoagulant) could not be obtained. Another limitation of the study is that due to its single-center design, subgroup analysis could not be performed in the vascular Behçet's group, in which vascular involvement of non-deep vein thrombus was rare. Therefore, the results of the study should be interpreted considering these situations. On the other hand, the most important strength of this study is that it provides detailed real-life data of patients with vascular BD.

This retrospective study found that vascular BD is more prevalent in men. The most common form of involvement in our patient group was deep vein thrombosis, consistent with previous studies. Additionally, this study showed that immunosuppressive drugs are the primary treatment for vasculo-BD, and anticoagulant therapy is frequently used in practice despite conflicting evidence. Additionally, there is a need for prospectively designed cohort studies and basic science research to determine the duration of immunosuppressive therapy and the effectiveness of anticoagulant therapy.

References

1. Hatemi G, Seyahi E, Fresko I, Talarico R, Uçar D, Hamuryudan V. Behçet's syndrome: one year in review 2022. Clin Exp Rheumatol 2022;40(8):1461-1471.
2. Emmi G, Bettiol A, Silvestri E, et al. Vascular Behçet's syndrome: an update. Internal and Emergency Medicine 2019;14:645-652.
3. Ishido T, Horita N, Takeuchi M, et al. Clinical manifestations of Behçet's disease depending on sex and age: results from Japanese nationwide registration. Rheumatology 2017;56(11):1918-1927.
4. Torgutalp M, Sahin Eroglu D, Sezer S, et al. Analysis of vascular involvement in 460 patients with Behçet's syndrome: Clinical characteristics and associated factors. Joint Bone Spine Mar 2022;89(2):105277.
5. Bettiol A, Alibaz-Oner F, Direskeneli H, et al. Vascular Behçet syndrome: from pathogenesis to treatment. Nature Reviews Rheumatology 2023;19(2):111-126.
6. Yazici H, Seyahi E. Behçet syndrome: the vascular cluster. Turkish journal of medical sciences 2016;46(5):1277-1280.
7. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis Jun 2018;77(6):808-818.
8. Alibaz-Oner F, Direskeneli H. Management of vascular Behçet's disease. Int J Rheum Dis Jan 2019;22 Suppl 1:105-108.
9. Tascilar K, Melikoglu M, Ugurlu S, Sut N, Caglar E, Yazici H. Vascular involvement in Behçet's syndrome: a retrospective analysis of associations and the time course. Rheumatology (Oxford) Nov 2014;53(11):2018-2022.
10. Fei Y, Li X, Lin S, et al. Major vascular involvement in Behçet's disease: a retrospective study of 796 patients. Clin Rheumatol Jun 2013;32(6):845-852.
11. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. Lancet May 5 1990;335(8697):1078-1080.
12. Düzgün N, Ateş A, Aydintuğ O, Demir Ö, Ölmez Ü. Characteristics of vascular involvement in Behçet's disease. Scandinavian journal of rheumatology 2006;35(1):65-68.
13. Ideguchi H, Suda A, Takeno M, Ueda A, Ohno S, Ishigatsubo Y. Characteristics of vascular involvement in Behçet's disease in Japan: a retrospective cohort study. Clin Exp Rheumatol 2011;29(4):47-53.
14. Merashli M, Ster IC, Ames PR. Subclinical atherosclerosis in Behcet's disease: A systematic review and meta-analysis. Semin Arthritis Rheum 2016;45(4):502-510.
15. Seyahi E, Ugurlu S, Cumali R, et al. Atherosclerosis in Behçet's Syndrome. Seminars in Arthritis and Rheumatism 2008;38(1):1-12.

16. Ugurlu S, Seyahi E, Yazici H. Prevalence of angina, myocardial infarction and intermittent claudication assessed by Rose Questionnaire among patients with Behcet's syndrome. Rheumatology 2008;47(4):472-475.
17. Kaymaz S, Yilmaz H, Furkan U, et al. Ultrasonographic measurement of the vascular wall thickness and intima-media thickness in patients with Behçet's disease with symptoms or signs of vascular involvement: a cross-sectional study. Archives of Rheumatology 2021;36(2):258.
18. Bettiol A, Hatemi G, Vannozzi L, Barilaro A, Prisco D, Emmi G. Treating the Different Phenotypes of Behçet's Syndrome. Front Immunol 2019;10:2830.
19. Alibaz-Oner F, Karadeniz A, Ylmaz S, et al. Behçet disease with vascular involvement: effects of different therapeutic regimens on the incidence of new relapses. Medicine 2015;94(6):e494.
20. Desbois A, Wechsler B, Resche-Rigon M, et al. Immunosuppressants reduce venous thrombosis relapse in Behçet's disease. Arthritis & Rheumatism 2012;64(8):2753-2760.
21. Ozguler Y, Hatemi G, Cetinkaya F, et al. Clinical course of acute deep vein thrombosis of the legs in Behçet's syndrome. Rheumatology 2020;59(4):799-806.
22. Alibaz-Oner F, Vautier M, Aksoy A, et al. Vascular Behçet's disease: a comparative study from Turkey and France. Clin Exp Rheumatol 2022;40(8):1491-1496.