VALIDATION STUDIES





Validity and reliability of a checklist for patients with Behçet's disease based on the International Classification of Functioning, Disability and Health

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Received: 30 July 2021 / Accepted: 15 September 2021 / Published online: 22 September 2021 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2021

Abstract

In 2020, we reported the "BD-checklist 92" for patients with Behçet's disease (BD) based on the International Classification of Functioning, Disability and Health. The purpose of the present study was to evaluate the validity and reliability of this checklist. Questionnaires using the "BD-checklist 92" and the 36-item Short Form Survey (SF-36) were sent to ten affiliated institutions. In total, 174 patients answered the questionnaire (response rate, 32.7%). Criterion validity was evaluated using the correlation coefficient between the number of problem categories extracted from the "BD-checklist 92" and the scores of the eight subscales and two components of the SF-36. Construct validity was assessed based on the number of problem categories extracted as an external criterion for the number of manifestations experienced and specific lesions. The comparison was performed using the Mann–Whitney U test. Cronbach's alpha coefficient was used to evaluate reliability. The number of problem categories in the "Body functions and structures", "Activities and participation", and "Environmental factors" components correlated significantly with all dimensions of the SF-36 questionnaire (P < 0.05 each). Construct validity showed that the number of manifestations experienced in all components (P < 0.001 each) and specific lesions in "Body functions and structures" and "All categories" (P = 0.002 and 0.050, respectively) contributed to an increased number of problems associated with BD. Cronbach's alpha coefficient for the "BD-checklist 92" was 0.926. This study confirmed the validity and reliability of the "BD-checklist 92".

Keywords Behçet's disease · Checklist · International Classification of Functioning, Disability and Health · Physical and psychosocial problems

Introduction

Behçet's disease (BD) is a systemic chronic inflammatory disease that shows repeated periods of symptom activity and inactivity [1]. In addition, patients with BD are aging in Japan [2]. As a result, the disease involves the physical and psychosocial problems of both the various symptoms of

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BD and aging. Assessment of the physical and psychosocial problems of patients with BD is, therefore, needed not only from the perspective of BD, but also for problems that occur during life in general.

To assess disease activity in patients with BD, the BD Current Activity Form (BDCAF) [3] instrument has been used, but it does not provide a framework for discussion in meetings of health-care providers from various disciplines regarding treatment plans and medical care for patients with BD. Furthermore, the BDCAF is not meant to measure psychosocial or social problems associated with treatment of patients with BD. As patients with BD need comprehensive support from a bio-psycho-social perspective, intervention by a multi-disciplinary team is needed.

In 2020, to identify physical and psychosocial problems based on symptoms of BD in Japanese patients, we developed and reported the "BD-checklist 92" for patients with BD based on the International Classification of Functioning,

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Disability and Health (ICF) [4]. This checklist can widely assess physical and psychosocial problems in patients with BD. Whereas the BDCAF evaluates disease activity, our checklist allows the identification of specific problems, providing medical staff with the opportunity to formulate treatment plans and medical care plans taking into account the problems that patients with BD are actually experiencing. However, the validity of this checklist has yet to be evaluated, preventing its application in clinical settings. Accordingly, this checklist needs to be confirmed as an index that can precisely evaluate the physical and psychosocial problems experienced by patients with BD.

The purpose of this study was, therefore, to evaluate the validity and reliability of the "BD-checklist 92" for patients with BD.

Material and methods

Data collection and procedures

In 2019, a questionnaire using the "BD-checklist 92" we sent to ten institutions to which members of the "Behçet's Disease Research Committee, Health and Labour Sciences Research Grants (Research on Intractable Diseases) from the Ministry of Health, Labour and Welfare of Japan" belong. The questionnaire form was handed by primary physicians to patients with BD visiting the participating medical institution. The survey was conducted from October 2019 to March 2020. In total, 174 patients answered the questionnaire (response rate, 32.7%). Of the 174 respondents, 23 were "suspected or possible BD disease" or "unknown". They were excluded from the analysis. The 151 patients analyzed fulfilled either "complete BD" or "definitive BD", which is the BD diagnostic standard of the Ministry of Health, Labor and Welfare [5].

Approvals were received from the Teikyo University Review Board (approval number 19-058).

Instruments

The "BD-checklist 92" included the following categories from the ICF: 33 categories from the "Body functions" component, 8 categories from the "Body structures" component, 31 categories from the "Activities and participation" component, and 20 categories from the "Environmental factors" component [4].

The 36-Item Short Form Survey (SF-36) [6] is a very popular instrument for evaluating Health-Related Quality of Life (QOL). The SF-36 measures eight subscales: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Component analyses have shown that two distinct concepts are measured by the SF-36: a physical dimension, represented by the Physical Component Summary and a mental dimension, represented by the Mental Component Summary [6]. The Japanese version was developed by Fukuhara et al. [7, 8].

Statistical analysis

Validity of the "BD-checklist 92" was assessed by evaluating both criterion validity and construct validity. Reliability was evaluated using Cronbach's alpha coefficient.

Criterion validity was evaluated using the correlation coefficient between the number of problem categories extracted from the "BD-checklist 92" and the scores of the eight subscales and two components of the SF-36. Spearman's correlation coefficient was used to evaluate the correlations. Examination of correlations with the BDCAF, which evaluates BD activity, would have been optimal, but no Japanese version of BDCAF has been developed, so the SF-36 was used as a proxy in this study.

Construct validity was evaluated by examining known group validity. The purpose of evaluating construct validity was to ascertain whether QOL based on the presence of various symptoms with BD and specific lesions of BD could be used to discriminate between groups known or expected to differ either clinically or in terms of QOL. Patients with BD were grouped according to the number of manifestations experienced and the specific lesions of BD for comparisons. The number of manifestations experienced was divided into <5 symptoms and \geq 5 symptoms, and the specific lesions of BD were compared according to their presence or absence. Comparisons were performed using the Mann–Whitney *U* test.

To evaluate internal consistency in all categories, Cronbach's alpha coefficient was calculated, and reliability assessments were performed.

Statistical analysis was performed using SPSS statistical software (SPSS Statistics Desktop for Microsoft Windows version 24.0; IBM, Armonk, NY). A P value < 0.05 was considered significant.

Results

Characteristics of patients

Characteristics of the 151 patients are shown in Table 1. Mean age was 52 years, and mean duration of BD was 15.3 years. The most frequent symptoms experienced were oral ulcers in 97.4% of patients, eye involvement in 72.2%, skin involvement in 69.5%, arthritis in 68.9%, genital ulcers in 66.9%, and fatigue in 62.9%. In terms of type, more than half of the patients were classified with definitive BD

Table 1 Clinical characteristics of patients

Characteristics	n (151)	Mean	SD
Sex (male/female) [n]	71/80		
Age (years)		52	14
Duration of BD (years)		15.3	11.8
Age at onset of BD (years)		36	10
Number of manifestations experienced		4.4	1.4
Manifestations experienced			
Oral ulcers $[n (\%)]$	147 (97.4)		
Genital ulcers $[n(\%)]$	101 (66.9)		
Eye involvement $[n (\%)]$	109 (72.2)		
Skin involvement $[n (\%)]$	105 (69.5)		
Arthritis [n (%)]	104 (68.9)		
Fatigue [<i>n</i> (%)]	95 (62.9)		
Type of BD			
Complete BD $[n (\%)]$	60 (39.7)		
Definitive BD $[n (\%)]$	91 (60.3)		
Specific lesions $[n (\%)]$	49 (32.5)		
Intestinal BD [n (%)]	21 (42.8)		
Neurological BD $[n (\%)]$	17 (34.7)		
Vascular BD $[n (\%)]$	11 (22.4)		
Number of problem category			
Body functions and structures		10.5	4.4
Activities and participation		8.2	6.8
Environmental factors		3.6	2.6
All components		22.3	11.8
SF-36 scores			
Physical functioning		78.4	24.1
Role physical		70.7	26.8
Bodily pain		63.8	21.3
General health		45.7	20.6
Vitality		51.5	14.5
Social functioning		73.6	26.9
Role emotional		73.0	27.7
Mental health		62.1	21.1
Physical components		40.8	21.9
Mental components		45.6	8.4

BD Behçet's disease, *n* number, *SD* standard deviation, *SF-36* 36-item Short Form Survey

(60.3%). Among patients with specific lesions (32.5% of all patients with BD), their types were intestinal BD in 42.8%, neurological BD in 34.7%, and vascular BD in 22.4%.

Criterion validity (Table 2)

We analyzed the relationship between the number of problem categories in each component of the "BD-checklist 92" and scores on dimensions of the SF-36 questionnaire to assess criterion validity. The number of problem categories in the "Body functions and structures" component correlated significantly with all dimensions of the SF-36 questionnaire (P < 0.01 each). Similarly, in the "Activities and participation" and "Environmental factors" components, significant associations were also found between the number of problem categories and scores in all dimensions of the SF-36 (P < 0.05 each).

Construct validity (Table 3)

First, patients with BD were divided into two groups based on the number of manifestations experienced; ≥ 5 manifestations experienced; or <5 manifestations experienced. The group with ≥ 5 manifestations showed a significantly greater number of problem categories than the group with <5 manifestations in all components (P < 0.001 each; Table 3).

Next, patients with BD were also divided into groups according to the presence or absence of specific lesions. Mean numbers of problem categories for "Body functions and structures" component and "All categories" were significantly higher in patients with specific lesions (P = 0.002 and 0.050, respectively).

Reliability (Table 4)

To evaluate the internal consistency of all categories, Cronbach's alpha coefficient values were calculated. Cronbach's alphas coefficients for "Body functions and structures", "Activities and participation", "Environmental factors" components, and "All categories" were 0.764, 0.917, 0.713, and 0.926, respectively.

Discussion

The present results demonstrate that the "BD-checklist 92" is a valid and reliable tool for identifying problems experienced by patients with BD in Japan. To the best of our knowledge, this represents the first study to develop a checklist for identifying physical and psychosocial problems of patients with BD using the ICF. Using this checklist, medical staff can precisely assess the physical and psychosocial problems that patients with BD are currently experiencing, enabling the development of a medical treatment plan and care plan to improve the physical and psychosocial problems associated with symptoms in these patients.

First, criterion validity of the "BD-checklist 92" was assessed against other standard measurements. To establish criterion validity, the SF-36 questionnaire was selected, and whether the number of problem categories in each component of the "BD-checklist 92" would correlate with each

Components	Dimensions									
	Physical functioning		Role physical		Bodily pain		General health		Vitality	
	r	Р	r	Р	r	Р	r	Р	r	Р
Body functions and structures	-0.544	< 0.001	-0.603	< 0.001	-0.358	< 0.001	-0.455	< 0.001	-0.390	< 0.001
Activities and participation	-0.449	< 0.001	-0.476	< 0.001	-0.228	0.005	-0.346	< 0.001	-0.226	0.005
Environmental factors	-0.534	< 0.001	-0.500	< 0.001	-0.153	0.060	-0.420	< 0.001	-0.271	0.001
All categories	-0.573	< 0.001	-0.594	< 0.001	-0.272	0.001	-0.439	< 0.001	-0.310	< 0.001
Components	Dimensions									
	Social functioning		Role emotional		Mental health		Physical compo- nents		Mental components	
	r	Р	r	Р	r	Р	r	Р	r	Р
Body functions and structures	-0.482	< 0.001	-0.443	< 0.001	-0.344	< 0.001	-0.527	< 0.001	-0.238	0.003
Activities and participation	-0.455	< 0.001	-0.349	< 0.001	-0.358	< 0.001	-0.492	< 0.001	-0.177	0.030
Environmental factors	-0.493	< 0.001	-0.353	< 0.001	-0.376	< 0.001	-0.519	< 0.001	-0.218	0.007
All categories	-0.530	< 0.001	-0.437	< 0.001	-0.417	< 0.001	-0.582	< 0.001	-0.222	0.006

Table 2 Spearman correlation coefficients between the number of the problem category in each component of the "BD-checklist 92" and scores on dimensions of the SF-36 questionnaire

BD Behçet's disease, SF-36 36-item Short form survey

Table 3Comparison of thenumber of the problem categoryin each component of the"BD-checklist 92" in number ofmanifestations experienced andspecific lesions

Components	Number of rienced	manifestation	s expe-	Specific lesions		
	<5 n=74	$ \geq 5 \\ n = 77 $	Р	Applicable $n = 49$	Not applicable $n = 102$	Р
Body functions and structures	8.0 ± 2.9	13.0 ± 4.1	< 0.001	12.2 ± 4.7	9.8±4.0	0.002
Activities and participation	6.1 ± 5.7	10.1 ± 7.2	< 0.001	8.6 ± 6.3	8.0 ± 7.0	0.335
Environmental factors	2.7 ± 2.1	4.5 ± 2.7	< 0.001	4.0 ± 2.7	3.4 ± 2.5	0.136
All categories	16.8 ± 8.8	27.6 ± 12.0	< 0.001	24.8 ± 12.3	21.1 ± 11.5	0.050

The Mann-Whitney U test was used for comparisons

BD Behçet's disease, n number

Table 4 Internal consistency of the "BD-checklist 92"

Components	Cronbach's α			
Body functions and structures	0.764			
Activities and participation	0.917			
Environmental factors	0.713			
All components	0.926			

BD Behçet's disease

subscale of the SF-36 was tested. It was found that none of the scores for the dimensions of the SF-36 and the number of problem categories extracted from each component of the "BD-checklist 92" showed a correlation coefficient of ≥ 0.6 . This may be because the evaluation items of the SF-36 are not items for specific diseases, whereas the "BD-checklist 92" is specific for BD, so the correlation between each item is strong. Therefore, there may not be a strong correlation between scores on dimensions of the SF-36 and the number of problem categories extracted from each component of the "BD-checklist 92". However, SF-36 score was shown to decrease as the number of problem categories in all components of the "BD-checklist 92" increased. This means that the problem categories extracted by the "BD-checklist 92" correlate with QOL in patients with BD.

Physical and psychosocial problems in patients with BD are known to lead to decreases in QOL [8, 9]. For example, Khabbazi et al. [9] demonstrated significant correlations between physical and mental health scores and most SF-36 domains with disease activity and clinical symptoms, including genital ulcers, ophthalmic involvement and central nervous system involvements (P < 0.05). Moreover, Aflaki et al. [10] showed that overall higher disease activity can be associated with lower QOL in patients with BD. In fact, the relationship in which QOL decreases as the number of problem categories extracted by the "BD-checklist 92" increases suggest that the present results are reasonable. In other words, this suggests that addressing the physical and psychosocial problems related to the treatment and symptoms of BD extracted from the "BD-checklist 92" may improve QOL in patients with BD. Therefore, the "BD-checklist 92" can be applied as a valid checklist from the perspective of QOL in patients with BD.

Second, to evaluate construct validity, patients with BD were divided into two groups based on the number of manifestations experienced and the presence or absence of specific lesions. Many symptoms and specific lesions are known to impact QOL negatively [11–13]. If the composition of the "BD-checklist 92" is appropriate, we hypothesized that patients who experience many manifestations, and patients with specific lesions will also experience problems in more categories. The present study confirmed that patients who experience problems in more categories experience problems in more categories than patients with specific lesions will also experience that patients with specific lesions will also experience that patients who experience problems in more categories than patients with specific lesions with specific lesions and patients with specific lesions with specific lesions and patients with specific lesions experience problems in more categories than patients who did not.

BD can show a wide variety of symptoms, such as oral ulcers [14–16], genital ulcers [15, 16], eye involvement [4, 15–17], skin involvement [15, 16, 18], arthritis [18, 19], and fatigue [4, 20]. The QOL of patients with BD who experience multiple symptoms, therefore, tends to be decreased compared to those with fewer symptoms [11]. In a study from the United Kingdom, seven of the ten symptoms assessed were associated with significant decrements in health-related QOL [11]. The present study divided the number of symptoms experienced into < 5 and ≥ 5 and compared the numbers of problem categories extracted from the "BDchecklist 92". The group with ≥ 5 symptoms experienced significantly higher numbers of problem categories for all "Body functions and structures", "Activities and participation", and "Environmental factors" components when compared with the group that experienced < 5 symptoms.

Moreover, BD includes specific lesions of neurological BD [21, 22], vascular BD [21, 23], and intestinal BD [24, 25]. Specific lesions affect the QOL of patients [12, 13]. Kuzu Kumcu et al. [12] reported that patients with neurological BD had significantly lower SF-36 scores in physical functioning, physical difficulty, bodily pain, and general health perception components compared with healthy controls. In a cross-sectional study in Iraq, a weak positive correlation was seen between vascular involvement and the total SF-36 score [13]. Similarly, in the present study, the number of problem categories extracted was greater in the group with specific lesions than in the group without specific lesions. In particular, significantly more problem categories were extracted in the "Body functioning and structures" component and in "All categories". This may be related to the fact that intestinal BD was the most common of the specific lesions in the present study (42.8%). Intestinal BD presents with symptoms such as abdominal pain, diarrhea, mucous feces, and hematochezia [25, 26]. These symptoms cause both physical and psychological discomfort. Although not a study of patients with intestinal BD, physical symptoms have been reported to decrease the QOL of patients with similar intestinal disorders [27-30]. In Crohn's disease, Guloksuz et al. [27] reported that Crohn's disease can change QOL, especially during flares, and it may cause major changes in the physical, emotional and social lives of patients. Moreover, Tomazoni et al. [28] demonstrated that Crohn's disease has a significant impact on patient QOL, particularly when symptoms are exacerbated, and contributes to the appearance of anxiety and/or depressive symptoms. In addition, in irritable bowel syndrome, Markland et al. [29] found that women with irritable bowel syndrome and fecal incontinence had poorer condition-specific QOL for fecal incontinence and other colorectal symptoms. Furthermore, Ozer et al. [30] showed that QOL seemed significantly lower in patients with irritable bowel syndrome-like symptoms than in those without such symptoms (P < 0.001). However, no significant difference was found in the components of "Activities and participation" and "Environmental factors". This may be because specific lesions were divisible into three groups (intestinal BD, neurological BD, and vascular BD), and comparisons with the group without specific lesions were not performed.

Cronbach's alpha coefficients for "Body functioning and structures", "Activities and participation", "Environmental factors" components, and "All categories" were 0.764, 0.917, 0.713, and 0.926, respectively. Since all components showed appropriate values, the reliability of the "BD-check-list 92" can be considered high.

Limitation

The present study had several limitations. First, since answers to the survey were based on the recall of the participants, the results may be prone to recall bias. Second, the response rate for the mail survey was low, at 32.7%. This may be a limitation inherent to mail surveys. Confirmation reproducibility may be best determined in a second interview. Third, the sample size was limited. Since the medical institutions that agreed to cooperate in the survey were concentrated in Tokyo and surrounding suburbs, 78.8% of respondents were patients living in Tokyo or its suburbs, which might have limited the generalizability of the results. Fourth, Cronbach's alpha coefficient was the only measure used to assess reliability. To evaluate reproducibility, a test–retest method should be used.

Conclusion

In conclusion, the present study demonstrated some degree of validity (criterion and construct validity) and reliability (Cronbach's alpha coefficient) of the "BD-checklist 92". This checklist is thus considered to provide an index to assess the physical and psychosocial problems experienced by patients with BD.

Acknowledgements This study was supported by JSPS KAKENHI Grant Number 16K04187. The authors would like to thank Associate Professor Y. Kirino from the Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine; Associate Professor H. Nagafuchi from the Departments of Rheumatology and Allergy, St. Marianna University School of Medicine; Clinical Associate Professor K. Namba from the Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University; Professor T. Sawada from the Department of Rheumatology, Tokyo Medical University; Clinical Associate Professor T. Tono from the Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine; Professor K. Nakamura from the Department of Dermatology, Saitama Medical University; Professor N. Kitaichi from the Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University; Visiting Professor S. Hirohata from the Division of Rheumatology and Allergy, Department of Internal Medicine, Teikyo University School of Medicine; and Health and Labour Sciences Research Grants (Research on Intractable Diseases) from the Ministry of Health, Labour and Welfare of Japan, for their support with respect to the mail survey.

Funding This study was supported by JSPS KAKENHI Grant Number 16K04187.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

References

- Sakane T, Takeno M, Suzuki N, Inaba G (1999) Behçet's disease. N Engl J Med 341:1284–1291. https://doi.org/10.1056/NEJM1 99910213411707
- Ministry of Health, Labour and Welfare (2021) Report on Public Health Administration and Services FY2019. https://www.e-stat. go.jp/stat-search/files?page=1&layout=datalist&toukei=00450 027&tstat=000001031469&cycle=8&tclass1=000001148807& tclass2=000001148808&tclass3=000001148810&cycle_facet= tclass1%3Atclass2%3Atclass3%3Acycle&tclass4val=0. Accessed 28 Mar 2021 (in Japanese)
- Bhakta BB, Brennan P, James TE, Chamberlain MA, Noble BA, Silman AJ (1999) Behçet's disease: evaluation of a new instrument to measure clinical activity. Rheumatology 38:728–733. https://doi.org/10.1093/rheumatology/38.8.728
- Tsutsui H, Kikuchi H, Oguchi H, Nomura K, Ohkubo T (2020) Identification of physical and psychosocial problems based on symptoms in patients with Behçet's disease. Rheumatol Int 40:81– 89. https://doi.org/10.1007/s00296-019-04488-1
- Japan Intractable Diseases Information Center (2020) Behçet's disease (Designated intractable disease 56). https://www.nanby ou.or.jp/entry/330. Accessed 16 Jul 2021 (in Japanese)
- Ware JE Jr, Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 30:473–483
- 7. Fukuhara S, Bito S, Green J, Hsiao A, Kurokawa K (1998) Translation, adaptation, and validation of the SF-36 Health Survey for

use in Japan. J Clin Epidemiol 51:1037–1044. https://doi.org/10. 1016/s0895-4356(98)00095-x

- Fukuhara S, Ware JE Jr, Kosinski M, Wada S, Gandek B (1998) Psychometric and clinical tests of validity of the Japanese SF-36 Health Survey. J Clin Epidemiol 51:1045–1053. https://doi.org/ 10.1016/s0895-4356(98)00096-1
- Khabbazi A, Ebrahimzadeh Attari V, Asghari Jafarabadi M, Malek MA (2021) Quality of life in patients with Behçet disease and its relation with clinical symptoms and disease activity. Reumatol Clin 17:1–6. https://doi.org/10.1016/j.reuma.2019.03.002
- Aflaki E, Farahangiz S, Salehi A (2020) Quality of life assessment in patients with Behçet's disease using the Persian version of the Leeds BD-QoL questionnaire. Iran J Med Sci 45:352–358
- Bernabé E, Marcenes W, Mather J, Phillips C, Fortune F (2010) Impact of Behçet's syndrome on health-related quality of life: influence of the type and number of symptoms. Rheumatology (Oxford) 49:2165–2171. https://doi.org/10.30476/ijms.2020. 72634.0
- Kuzu Kumcu M, Bakırarar B, Yücesan C (2021) Quality of life in neuro-Behçet's disease: a cross-sectional study. Neurol Sci 42:1081–1086. https://doi.org/10.1007/s10072-020-04630-z
- Gorial FI, Jabbar MA (2020) Impact of disease activity on health related quality of life in patients with Behçet's disease: a crosssectional study. Ann Med Surg (Lond) 54:43–46. https://doi.org/ 10.1016/j.amsu.2020.03.010
- Taylor J, Glenny AM, Walsh T et al (2014) Interventions for the management of oral ulcers in Behçet's disease. Cochrane Database Syst Rev 25:CD011018. https://doi.org/10.1002/14651858.CD011 018.pub2
- Scherrer MAR, Rocha VB, Garcia LC (2017) Behçet's disease: review with emphasis on dermatological aspects. An Bras Dermatol 92:452–464. https://doi.org/10.1590/abd1806-4841.20177 359
- Zhang J, Tang Y, Yue S et al (2019) A review of Behçet's disease from the perspectives of both Western and Chinese medicine. J Tradit Chin Med 39:139–152
- Ksiaa I, Abroug N, Kechida M et al (2019) Eye and Behçet's disease. J Fr Ophtalmol 42:e133–e146
- Leccese P, Ozguler Y, Christensen R et al (2019) Management of skin, mucosa and joint involvement of Behçet's syndrome: a systematic review for update of the EULAR recommendations for the management of Behçet's syndrome. Semin Arthritis Rheum 48:752–762. https://doi.org/10.1016/j.semarthrit.2018.05.008
- Vaiopoulos AG, Kapsimali V, Kanakis MA et al (2019) The frequency of arthritis in Adamantiades-Behçet's disease in Greek patients. J Eur Acad Dermatol Venereol 33:416–420. https://doi. org/10.1111/jdv.15326
- Ilhan B, Can M, Alibaz-Oner F et al (2018) Fatigue in patients with Behçet's syndrome: relationship with quality of life, depression, anxiety, disability and disease activity. Int J Rheum Dis 21:2139–2145. https://doi.org/10.1111/1756-185X.12839
- Hirohata S, Kikuchi H (2003) Behçet's disease. Arthritis Res Ther 5:139–146. https://doi.org/10.1186/ar757
- Hirohata S (2015) Neurological involvement. In: Ishigatsubo Y (ed) Behçet's disease. From genetics to therapies. Springer Japan, Tokyo, pp 101–116
- Takeno M, Ideguchi H, Suda A, Kamiyama R, Ishigatsubo Y (2015) Vascular involvement of Behçet's disease. In: Ishigatsubo Y (ed) Behçet's disease. From genetics to therapies. Springer Japan, Tokyo, pp 79–100
- Nagahori M (2015) Gastrointestinal involvement. In: Ishigatsubo Y (ed) Behçet's disease. From genetics to therapies. Springer Japan, Tokyo, pp 117–127
- Ye JF, Guan JL (2019) Differentiation between intestinal Behçet's disease and Crohn's disease based on endoscopy. Turk J Med Sci 49:42–49. https://doi.org/10.3906/sag-1807-67

- Choi HJ, Seo MR, Ryu HJ, Baek HJ (2015) Cross-cultural adaptation and validation of the Behcet's disease current activity form in Korea. Korean J Intern Med 30:714–718. https://doi.org/10.3904/ kjim.2015.30.5.714
- 27. Guloksuz S, Wichers M, Kenis G et al (2013) Depressive symptoms in Crohn's disease: relationship with immune activation and tryptophan availability. PLoS ONE 8:e60435. https://doi.org/10. 1371/journal.pone.0060435
- Tomazoni EI, Benvegnú DM (2018) Symptoms of anxiety and depression, and quality of life of patients with Crohn's disease. Arq Gastroenterol 55:148–153. https://doi.org/10.1590/S0004-2803.201800000-26
- 29. Markland AD, Jelovsek JE, Rahn DD et al (2017) Irritable bowel syndrome and quality of life in women with fecal incontinence.

Female Pelvic Med Reconstr Surg 23:179–183. https://doi.org/10. 1097/SPV.000000000000358

 Ozer M, Bengi G, Colak R, Cengiz O, Akpinar H (2020) Prevalence of irritable bowel syndrome-like symptoms using Rome IV criteria in patients with inactive inflammatory bowel disease and relation with quality of life. Medicine (Baltimore) 99:e20067. https://doi.org/10.1097/MD.00000000020067

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