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ORIGINAL ARTICLE

Validity and reliability of the BODI for assessing damage in Behcet's disease

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Abstract

Objective In the present study, we aimed to validate the Behçet's syndrome Overall Damage Index (BODI) and compare its performance with that of vasculitis damage index (VDI) in Iranian patients with BD.

Methods This study included 274 patients with a diagnosis of BD and median follow-up of 40 months. The medical records of the patients were reviewed and the demographic characteristics, disease activity status, clinical manifestations, and data on organs damage were collected from all patients.

Results To evaluate the construct/convergent validity, BODI and VDI were applied to all participants. We found a good correlation between BODI score and VDI score. There was a significant and strong correlation between physician global assessment with BODI ($r=0.869$, $P=0.001$) and VDI ($r=0.817$, $P=0.001$). The ability of BODI to determine the accumulation of damage over time was assessed by analyzing the changes in BODI score over time. The increase in BODI score was occurred in 53 (19.3%) patients. In comparison, the increase in VDI score occurred in 36 (13.1%) patients. The increase in median BODI was significantly more than median VDI ($P<0.001$). Multiple linear regression analysis showed that age at disease onset, disease duration, and disease severity were independent predictors of BODI scores. Reliability of BODI was examined by comparing the BODI scores as determined by two independent assessors in 100 patients. Cronbach's α was 0.942.

Conclusion The BODI demonstrated acceptable validity and reliability in assessing BD-related damage in Iranian patients with BD.

Keywords Behcet's disease · Behçet's syndrome Overall Damage Index (BODI) · Damage · Vasculitis damage index (VDI)

Key points
- There was a significant and strong correlation between physician global assessment with BODI and VDI.
- Age at disease onset, disease duration, and disease severity were independent predictors of BODI scores.
- BODI demonstrated acceptable validity and reliability in assessing BD-related damage in Iranian patients with BD.

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Introduction

Behcet's disease (BD) is a vasculitis characterized by mucocutaneous lesions, ocular inflammation along with symptoms caused by involvement of the joints, vessels, central nervous system (CNS), epididymis, and gastrointestinal (GI) tract [1]. Due to the chronic and recurrent nature of BD, assessment of irreversible organ damage is an essential component of management and assessing prognosis of this disease in the daily practice [2, 3]. In addition, organ damage along with disease activity is part of the core set of endpoints recommended for clinical trials and longitudinal observational studies [2, 4].

Vasculitis damage index (VDI) is the most commonly used assessment tool for systemic vasculitides. The VDI consists of 11 subclasses and 64 items [5]. Every item has one score and higher scores shows more irreversible changes [5]. It has been mainly validated in anti-neutrophil

cytoplasmic antibody (ANCA) associated vasculitis and polyarteritis nodosa and lacks BD-specific items [5–7]. Therefore, VDI has significant limitations in measuring damage in BD [6, 7]. Recently, the Behçet's syndrome Overall Damage Index (BODI) group has developed and published an evidence-based and consensus-based damage index [8]. The BODI consists of 9 subclasses and 34 items [8]. Similar to VDI, every item has one score and higher scores shows more damage [8]. Each item must be lasted ≥ 6 months to be scored [8]. Preliminary results have shown the construction validity and reliability of BODI [8]. BODI was more sensitive than VDI in detecting major organ damage [8].

In the present study, we aimed to validate the BODI and compare its performance with that of VDI in Iranian patients with BD.

Methods

Study population

This study was designed and implemented in Connective Tissue Diseases Research Center to assess the ability of BODI to record the accumulation of damage over time. The study protocol was in compliance with the Helsinki declaration and was approved by the local Ethical committee. All patients with diagnosis of BD were screened consecutively for enrollment in this study between June 2021 and May 2022. Inclusion criteria were age ≥ 16; diagnosis of BD according ICBD [9], having at least two visits, and follow-up duration ≥ 1 years. The medical records of the patients were reviewed and the demographic characteristics, disease activity status, clinical manifestations, and data on organs damage were collected from all patients. BD activity was measured by the Behcet's disease current activity form (BDCAF) [10]. Severity of BD was determined based on the organs involved [11]. Patients with retinal vasculitis, posterior uveitis, pyoderma gangrenosum, cellulitis, GI bleeding, bowel perforation, deep vein thrombosis (DVT), vasculitis, and CNS involvement except headaches were classified as severe disease. Patients with oral ulcer, genital ulcer, erythema nodosum, pseudofolliculitis, superficial phlebitis, arthralgia, arthritis, headaches, epididymitis, recurrent diarrhea, and colicky abdominal pain were classified as mild diseases. We defined sustained remission as BDCAF < 1 for at least 6 months and using prednisolone with doses ≤ 5 mg/d [12, 13].

Validity and reliability assessment

Construct/convergence validity was determined by correlating BODI scores and its subclasses with VDI scores and its subclasses, disease severity and physician global assessment of damage (PGA-D). PGA-D scored on a scale visual analogue scale (VAS) of 0–10. Correlation coefficients ≥ 0.80 were considered very strong [14]. *Discriminant validity* of the BODI was determined by evaluating changes in BODI scores between the first and last visit. Furthermore, we analyzed the association between factors were expected to influence damage and disease outcome and BODI score [12, 13]. These factors were age at disease onset, disease duration, sex, disease severity, and remission status [14, 17]. *Reliability* was determined by correlating BODI scores as determined by 2 independent trained assessors and calculating Cronbach's α coefficient. A Cronbach's $\alpha \geq 0.70$ is generally is generally considered acceptable for reliability [15, 16].

Statistical analysis

The data obtained in this study were analyzed using the version 16 of IBM SPSS software. Qualitative data were reported as numbers and percentages and quantitative data as mean and standard deviation or median (25th and 75th percentiles). Spearman correlation test was used to evaluate the correlation, and the validity of the Behcet's disease damage index was compared with the VDI. A p-value less than 0.05 was considered statistically significant. Furthermore, a multiple linear regression analysis was performed to determine independent associations of BODI. P values less than 0.05 were considered as statistically significant.

Results

This study included 274 patients with a diagnosis of BD and median follow-up of 40 months. The demographic and clinical characteristics of the participants are summarized in Table 1. A BD-related damage was observed in 74 (27%) patients (Table 2, Fig. 1).

To evaluate the construct/convergent validity, BODI and VDI were applied to all participants. All assessments were performed by an expert rheumatologist. Then, the correlation of BODI score with VDI score was evaluated. We found a good correlation between BODI score and VDI score (Table 3). After that, we evaluated the correlation of BODI and VDI subclasses scores. There was a good correlation between BODI and VDI subclasses scores (Table 3). The highest correlation was between the ocular subscale of BODI and VDI (Table 3). It should be included that the head and neck, lower airway, and renal subclasses VDI do not exist in BODI and reproductive subclass of BODI does not exist in VDI. In addition, we assessed the correlation of BODI and VDI scores with PGA-D. There was a significant and strong correlation between PGA-D with BODI ($r = 0.869$, $P = 0.001$) and VDI ($r = 0.817$, $P = 0.001$). BD had a mild course in 147 (55.7%) and severe course in 127 (47.6%) patients. Median BODI scores in patients with severe and

Table 1 The demographic and clinical characteristics of participants ($N=274$)

Characteristics	Number
Male (%)	173 (63.1)
Age at the time of study, mean ± SD	41.9 ± 11.5
Oral aphthous ulcer (%)	263 (96.0)
Eye involvement (%)	133 (48.5)
Genital aphthous ulcer (%)	143 (52.2)
Positive pathergy test (%)	102 (37.2)
Pseudofolliculitis (%)	88 (32.1)
Erythema nodosum (%)	46 (16.8)
Arthritis (%)	75 (27.4)
Phlebitis (%)	39 (14.2)
CNS involvement (%)	15 (5.5)
Vasculitis (%)	8 (2.9)
Epididymitis (%)	9 (3.3)
Gastrointestinal involvement (%)	4 (1.5)
Severe disease (%)	127 (46.4)
BDCAF of the first visit, median (IQR)	2 (1, 2)
BDCAF of the last visit, median (IQR)	0 (0, 1)
Treatment with GCs (%)	228 (83.2)
Treatment with DMARDs (%)	213 (77.7)
Follow-up duration, median (IQR) months	40 (11, 90)

SD, Standard Deviation; *CNS*, Central Nervous System; *BDCAF*, Behcet's Disease Current Activity Form; *GC*, Glucocorticoids; *DMARDs*, Disease-modifying Antirheumatic Drugs; *IQR*, Interquartile Range

mild disease were 3 (range 0.25–5) and 0 (range 0–1), respectively. The differences were significant ($P=0.001$).

The ability of BODI to determine the accumulation of damage over time was assessed by analyzing the changes in BODI score over time. The median interval was 40 months (range 11–90 months). The increase in BODI score from cohort entry to last observation was occurred in 53 (19.3%) patients. The median BODI increased from 0 (range 0–2) at the baseline to 0 (range 0–3) at the last visit ($P<0.001$).

Table 2 Poor outcomes of patients with diagnosis of BD ($N=274$)

	Number
Cataract (%)	53 (19.3)
Decrease in visual acuity (%)	44 (16.1)
Blindness (%)	31 (11.3)
Osteoporosis (%)	7 (2.6)
Venous insufficiency (%)	5 (1.8)
Paresis, paralysis (%)	4 (1.5)
Avascular necrosis (%)	1 (0.4)
Dementia (%)	1 (0.4)
Death (%)	2 (0.7)

BD, Behcet's Disease

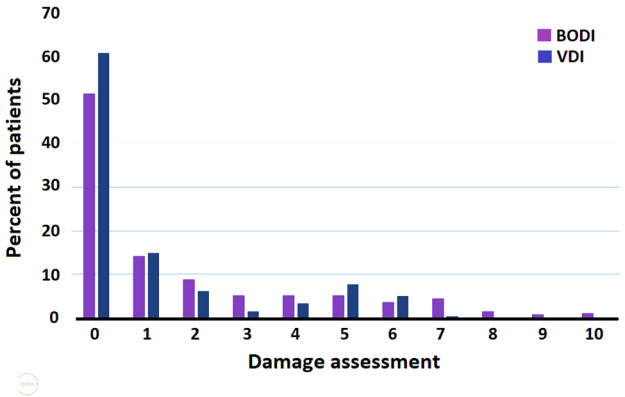

Fig. 1 Damage scores at last observation, as determined for 274 patients with Behcet's disease. VDI, vasculitis damage index; BODI, Behçet's syndrome Overall Damage Index

In comparison, the increase in VDI score occurred in 36 (13.1%) patients. The median VDI increased from 0 (range 0–1) at the baseline to 0 (range 0–2) at the last visit ($P<0.001$). The increase in BODI was significantly more than VDI ($P<0.001$). Then, we performed multiple linear regression analysis for assessing the association between BODI and parameters expected to influence damage (Table 4). Analysis showed that age at disease onset, disease duration, and disease severity were independent predictors of BODI scores after model adjustment for age at disease onset, disease duration, male sex, BMI, treatment with glucocorticoids, treatment with disease-modifying antirheumatic drugs, BDCAF, and disease severity (Table 4).

Reliability of BODI was examined by comparing the BODI scores as determined by two independent assessors in 100 patients. Cronbach's α was 0.942.

Table 3 Correlation between BODI and VDI

	Pearson correlation	*P*-value
Total BODI versus VDI	0.941	0.001
Subclasses of BODI versus VDI		
Mucocutaneous	0.852	0.001
Musculoskeletal	0.796	0.001
Ocular	0.970	0.001
Vascular	0.853	0.001
Cardiac*	-	-
Neuropsychiatric	0.793	0.001
Gastrointestinal	0.948	0.001
Miscellaneous*	-	-

*No patients scored in VDI subclass

BODI, Behçet's Syndrome Overall Damage Index; *VDI*, Vasculitis Damage index

Table 4 Multiple linear regression model of independent predictors for damage

Dependent variables	Predictors	Univariate analysis	Multivariate analysis			
		P-value	*β*	SE	*t*-value	*P*-value
BODI	Age at disease onset	0.004	-0.062	0.019	10.884	**0.010**
	Disease duration	0.001	-0.042	0.021	3.903	**0.048**
	Male sex	0.001	0.373	0.376	0.985	0.321
	BMI	0.231				
	Treatment with GCs (ever)	0.001	1.351	0.773	3.082	0.079
	Treatment with DMARDs (ever)	0.001	0.402	0.599	0.450	0.502
	BDCAF of the first visit	0.946				
	BDCAF of the last visit	0.001	-0.057	0.188	0.092	0.762
	Severe disease	0.001	1.922	0.449	18.332	**0.001**
	Sustained remission	0.001	0.050	0.187	0.072	0.788

BODI, Behcet's Syndrome Overall Damage Index; *SE*, Standard Error; *BMI*, Body Mass Index; *GCs*, Glucocorticoids; *DMARDs*, Disease-modifying Antirheumatic Drugs; *BDCAF*, Behcet's Disease Current Activity Form

Bolded data are independent predictors of damage

Discussion

BD has a waxing and waning course and, in most patients, the disease activity decrease with time and many patients' loss the criteria of BD and even become asymptomatic [13, 17]. However, irreversible organs damage especially eye, CNS and vascular system develop during attacks of disease [13, 17]. Damage indices are essential for assessing treatment efficacy and prognosis of chronic diseases like BD in clinical trials and daily practice [2–4]. Piga et al. developed the BODI in 2020 [8]. A preliminary study showed the validity of BODI [8]. In BODI validation cohort, the male-to-female ratio was 1 and the mean age at enrolment to study was 47 years [8]. Critical organs involvement including eye, nervous system, and vascular involvement were reported in 57, 21, and 23% of patients, respectively [8]. The median BDCAF was 1 [8]. In 56% of patients, at least one organ was damaged, so that the average BODI was 3 [8]. This study aimed to validate the BODI using Iranian patients' data. In our cohort, 63% of patients were male and the mean age at the time of study was 42 years. Although the frequency of eye involvement was comparable to Piga et al.'s study, the nervous system and vascular involvement were less frequent. The median BODI was 0 and damage occurred in 27% of patients.

The strong correlation ($r = 0.941$) between BODI and VDI and their subclasses especially the eye subclass showed *convergent validity* of BODI. Visual impairment is the most common morbidity of BD [18]. A retrospective study of 880 patients with BD reported that risk of blindness at 10 years for men and women was 30% and 17%, respectively [19]. Validity of eye subclass of BODI can be promising in assessing BD induced damage. An excellent correlation between PGA-D with BODI and higher BODI scores in BD patients with severe course further supported convergent validity of BODI. However, the low prevalence of certain types of damage limits the interpretation of comparisons of some subclasses of BODI and VDI.

The ability of BODI to determine the accumulation of damage over time, which was even better than VDI, demonstrated the *discrimination validity* of BODI. Independent association between BODI and predictors of poor outcome in BD including age at disease onset, disease duration, and disease severity [12, 13] along with lack of association between BD activity and BODI further supported the *discrimination validity* of BODI. Getting a high Cronbach's α in reliability analysis of BODI scores which determined by two independent assessors proved *reliability* of BODI.

Our study was strengthened by the relatively large sample size and long follow-up duration which increased the reliability of assessing damage accumulation over time. This study had several limitations. First, this study was retrospective. Second, the study was single center and all participants were followed at a university clinic which may led to selection bias, although our center is a referral center in northwestern Iran and most BD patients in this area are visited in BD clinic of our center. Third, data on several parameters such as quality of life assessment, disability index, and patient global assessment were not accessible.

Conclusion

The BODI demonstrated acceptable validity and reliability in assessing a BD-related damage in Iranian patients with BD. The BODI may be a useful and reliable tool for assessing irreversible changes in BD.

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Author contribution SM, AKH, and AMM designed the study; SM, RF, MR, and AKH were involved in the data acquisition and/or management; AKH and MG analyzed the data and critically interpreted the results; SM, RF, MR, and AKH were involved in drafting the manuscript. All authors revised the manuscript critically for important intellectual content and approved the final manuscript.

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Data Availability Data supporting the findings of this study are available from the corresponding author upon request.

Declarations

Competing interests The authors declare no competing interests.

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