Organ damage is a major determinant of work productivity impairment in Behçet's Syndrome: a post-hoc analysis of the BODI validation study

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ABSTRACT

OBJECTIVES

To evaluate the prevalence, magnitude, and potential determinants of work productivity impairment in patients with Behçet's Syndrome (BS), focusing on the role of irreversible organ damage.

METHODS

A post-hoc analysis of the BS overall damage index (BODI) prospective validation study was performed. Demographics and clinical features were recorded in all patients. The Work Productivity and Activity Impairment: General Health (WPAI: GH) questionnaire was administered to assess the work limitation and the BODI to measure organ damage. The independent effect of BS features on WPAI:GH outcomes was evaluated by regression analysis.

RESULTS

Out of 148 patients, 34.5% were unemployed, with age (OR 1.035) and BODI score (OR 1.313 for 1-unit increase) as the only factors significantly ($p < 0.05$) associated with the unemployment state. An overall work impairment was reported in about 64.2% of the employed patients. Indeed, 22.7% reported missing work hours due to their health (absenteeism), with a mean time loss of 34.4%; whereas 60.2% declared a reduced performance at work because of their health (presenteeism), with a mean productivity impairment of 45.4%. Ocular damage was associated with absenteeism (β 0.225); female sex (β 0.260), physician global assessment of disease activity (β 0.502) and an increased BODI score (β 0.166 for 1-point increase) with presenteeism; fibromyalgia (β 0.246), physician global assessment (β 0.469), and musculoskeletal damage (β 0.325) with overall work impairment.

CONCLUSIONS

Disease activity and organ damage accrual remarkably affect work productivity in BS patients. Achieving remission and preventing damage accrual are crucial and complementary objectives.

Keywords

Behçet's syndrome, work productivity, damage, outcomes.

Key messages

- Behçet's syndrome (BS) patients report a remarkable work productivity impairment.
- Work productivity impairment may persist in inactive disease and can be related to organ damage accrual.
- Achieving remission and preventing damage are crucial and complementary objectives in the management of BS.

INTRODUCTION

Behçet's Syndrome (BS) is a multisystem chronic inflammatory disorder characterized by a wide spectrum of clinical presentations, ranging from limited mucocutaneous lesions to life-threatening manifestations [1]. Because of its relapsing disease activity and the potential accrual of organ damage, BS can severely impact different physical, mental, and social aspects of the patient's daily life, resulting in significant impairment of quality of life [2,3]

Workability and productivity are increasingly recognised as important outcomes in patients with rheumatic diseases since they affect different domains of wellness [4]. Indeed, loss of work productivity impacts the patient's income level, economic independence, social role, standards of living, and overall quality of life [5,6]. Moreover, work limitation represents a major indirect social cost [7]. In patients affected by chronic diseases, the impact on production activities may include absence from work ("absenteeism"), a reduction in productivity, or the ease of work and producing (at-work productivity loss, "presenteeism") [4].

In previous studies, a low employment rate was described in BS patients, and multiple disease activity factors, especially mucocutaneous, articular, and ocular manifestations, were associated with productivity loss related to presenteeism and overall daily activity impairment [8,9]. However, no study has evaluated the role of irreversible organ damage when assessing the impact of BS on workability, which represents a critical limitation. Indeed, as in other relapsing and remitting diseases, persistent impairments in daily activity may occur because of the accrual of irreversible damage, even in BS patients experiencing clinical remission.

The present study aimed to evaluate the prevalence, magnitude, and potential determinants of impairment in workability and productivity in BS patients, focusing on the potential role of irreversible organ damage.

METHODS

Patients and study design

This is a cross-sectional post-hoc analysis of the follow-up phase of the BODI validation study [3], where a multicenter cohort of BS patients from Italy, Portugal, Spain and Greece was recruited according to the following criteria: (a) diagnosis of BS fulfilling the International Study Group (ISG) criteria or the International Criteria for Behçet's Disease (ICBD) [1], (b) disease duration ≥12 months, (c) age at enrolment ≥18 years and (d) ability to provide informed consent. Within the BODI validation cohort, patients with the available workability and productivity data, as assessed by the Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH) [4], were recruited for the present analysis. The study was approved by the Ethics Committee of the coordinating center at the AOU of Cagliari (Prot. PG/2018/17158, update 3rd September 2020). Written informed consent was obtained from all participants.

Data collection

Demographics, active and cumulative clinical manifestations, and ongoing medications were recorded, and the overall disease activity was assessed by Behçet's Disease Current Activity Form (BDCAF) [10], the Physician Global Assessment (PGA) [11], and the Patient Global Assessment (PtGA) [11] were recorded. The extent and type of organ damage accrual were assessed by the BS overall damage index (BODI), consisting of 34 items and 12 subitems, categorized into nine organ/system domains: mucocutaneous, musculoskeletal, ocular, vascular, cardiovascular, neuropsychiatric, gastrointestinal, reproductive system and miscellaneous [12].

Work-related outcomes

The WPAI:GH, a self-administrated questionnaire, was used to assess the employment rate and work productivity at a single time point. It comprises six questions exploring paid and unpaid work during the last seven days before the clinic appointment [13,14]. The following outcomes were determined and analyzed: 1) rate of patients employed for pay; 2) per cent work time missed due to health in currently employed patients (*absenteeism*); 3) per cent impairment while working due to health in patients who were currently employed and worked in the past seven days (*presenteeism*); 4) per cent overall work impairment due to health for those who were currently employed (combined absenteeism and presenteeism); 5) per cent *activity impairment* due to health for all respondents [13].

Statistical analysis

Categorical variables were expressed as absolute values and frequencies (%). Continuous variables are reported as the mean ± standard deviation (SD). The Spearman's correlation coefficient and T Student test or the Mann–Whitney *U*-test were used in univariate analysis to identify potential associations between BS features and WPAI: GH questionnaire scores. Variables with a p-value < 0.1 at the univariate analysis were selected, and logistic or multiple linear regression models (according to the nature of the dependent variable) were built to assess the independent effect of every single variable set on WPAI-GH outcomes: absenteeism, presenteeism, overall work impairment, and activity impairment. Statistical significance was set for p-value < 0.05.

RESULTS

Population

Of the 189 patients recruited in the follow-up phase of the BODI validation study, 148 (78.3%) were eligible for the present analysis (**Table 1**). Seventy-two (48.6%) were females. The mean age at the WPAI:GH assessment was 46.2 (±12.1) years and the mean disease duration was 13.9 (±9.9) years. Online **Supplementary Table S1, available at *Rheumatology* online,** reports attrition analysis with descriptive data for available baseline variables on included versus excluded patients.

Of the 148 patients enrolled for the present analysis, 97 (65.5%) stated they were working for pay. The remaining 51 (34.5%) patients were unemployed. At the multivariate analysis, the only factors independently associated with the unemployment status were the age at enrolment (1.035 per 1-year, 95%CI 1.002-1.068; p = 0.038) and the BODI score (OR 1.313 per 1-unit, 95%CI 1.051-1.640; p = 0.017) (**Supplementary Table S2, available at *Rheumatology* online,**).

Absenteeism and associated factors

Among the 97 BS patients working for pay, the mean percentage of work hours missed for health problems (absenteeism) was 7.9% (± 21.6). Out of the 97 employed patients, 22 (22.7%) reported missing at least one work hour, accounting for a mean missed working time of 34.4% (± 17.8) (**Figure 1a**).

In the multivariate analysis, only damage in the ocular BODI domain (β 0.225, $p = 0.027$) was independently associated with absenteeism **(Supplementary Table S2)**.

Presenteeism and associated factors

Ninety-three patients reported working for at least 1 hour the previous week. In this patient group, the mean per cent work productivity impairment due to health (presenteeism) was 27.3% (±30.7). Out of the 93 patients working for at least 1 hour in the previous week, 56 (60.2%) declared that health problems affected their work productivity, with a mean per cent impairment (presenteeism) of 45.4% (±27.2) (**Figure 1b**).

At the multivariate analysis, the female gender (β 0.260, p = 0.002), higher PGA (β 0.502, p < 0.001), and increased BODI score in the last two years' follow-up (β 0.166 for one-point increased BODI score, p = 0.046) were the only factors confirmed as independently associated with work impairment **(Supplementary Table S2)**.

Overall work impairment and associated factors

Among 95 employed patients (excluding those who did not work because of reasons other than health problems), the mean percentage of overall work impairment was 31.7 (± 33.4).

Of these 95 patients, 61 (64.2%) reported some per cent of overall work impediment due to their health, with a mean value of 49.6% (± 29.5).

In the multivariate analysis, fibromyalgia (β 0.246, p = 0.005), PGA (β 0.469, p < 0.001), and musculoskeletal damage (β 0.325, p < 0.001) were confirmed to be independently associated with overall work impairment **(Supplementary Table S2)**.

Impairment of daily activity and associated factors.

In the entire cohort of 148 patients, the mean percentage of daily activity impairment was 33.3 (± 30.6). In particular, 99 (66.9%) complained that health problems affected their ability to do regular daily activities other than work at a job, with a mean impairment of 49.8% (±23.9) (**Figure 1d**).

At multivariate analysis, female sex (β 0.145, p = 0.038) fibromyalgia (β 0.222, p = 0.002), higher disease activity assessed by the PGA (β 0.285, p = 0.001) and PtGA (β 0.323, p = 0.004) were identified as factors significantly associated with daily activity impairment **(Supplementary Table S2)**.

DISCUSSION

This study analyzed the extent and potential determinants of work productivity impairment in BS patients, providing meaningful and original data regarding the critical role of irreversible organ damage.

A low employment rate was recorded in our BS cohort, as in a previous study by Karacayli U et al. [8]. Although a comparison with a control group is not available, our analysis suggests a significant impact of organ damage on the unemployment rate since a greater damage accrual was recorded in the unemployed patients. Moreover, this assumption is further supported by the fact that several disease-related factors were found to be major determinants of work limitations in employed patients.

Our cohort recorded a high prevalence and magnitude of absenteeism, presenteeism, and overall work impairment among the employed patients since about two-thirds reported missing work time or productivity loss. All three work-related outcomes were found to be affected by organ damage assessed by the BODI.

Concerning absenteeism, the only associated factor was ocular damage. This highlights how eye involvement has a great impact on critical aspects of a patient's daily life, including workability [1,3]

When the potential determinants of presentism were assessed, we found that, besides gender and disease activity, a recent increase in organ damage over time significantly impacts the patient's productivity. Notably, the accrual of organ damage, rather than its extent assessed in a single visit, was associated with presenteeism. Such an observation may be explained by coping mechanisms that may occur in patients with stable damage but may not yet be developed in the presence of recent damage accrual [3].

Regarding the determinants of overall work impairment, we clearly observed how this outcome was significantly affected by disease activity and organ damage. In particular, we found that musculoskeletal damage had a remarkable impact probably because it may significantly impact perceived efficiency and productivity at work, although it does not entirely prevent working.

Finally, our study showed that three-quarters of the interviewed patients reported health problems affecting their ability to do regular daily activities. In this case, the lack of an independent association with damage may be due to the more generic nature of the investigated outcome, which may be more

affected by self-perceived aspects of the general quality of life rather than objective and specific aspects of BS.

To date, few studies have analyzed the impact of BS on work productivity. Mumuc G et al. recorded values of absenteeism and presentism similar to ours (9% and 31%, respectively) in a multicenter cohort of BS patients from Jordan, Brazil, the United Kingdom, and Turkey [9]. This study found several active disease manifestations as primary determinants of work limitations, including oral and genital ulcers and joint and eye involvement [9]. These data are meaningful, as they demonstrated how active BS manifestations, even those commonly considered mild, impact the patient's workability and productivity. However, these studies did not analyze organ damage, a critical outcome in diseases with a relapsing-remitting course like BS, as patients may experience significant work limitations during the inactive disease state.

After the demonstration of the reliability, sensitivity to change, and feasibility of the BODI during its preliminary validation [12] and in further independent cohorts from Iran, Egypt, and Turkey [15–17], the demonstration of its correlation with work productivity, provides significant evidence in support of its criterion validity. Such evidence, unavailable for other instruments [18], further encourages using the BODI as the only validated measure of damage for BS patients in clinical practice and research.

Some limitations of this study should be acknowledged. First, the long-standing nature of the studied cohort and the relatively low proportion of very active patients might have reduced the sensitivity in identifying the role of some active manifestations in the work impairment in BS. On the other hand, this feature of our cohort highlights how patients in remission or with mild disease activity may experience a remarkable impairment in their work productivity. Second, comparison with other vasculitis and further validation of our results in more extensive and ethnically heterogeneous cohorts is needed since they may be influenced by socioeconomic and welfare in different country areas.

In conclusion, due to disease activity and damage accrual, BS can significantly impair the patient's work productivity. Achieving remission and preventing damage accrual are crucial and complementary outcomes in BS, as they impact other critical domains of the patient's well-being.

DECLARATION SECTION

Declaration of competing interests: The authors have declared no conflicts of interest.

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Data Availability Statement: The study dataset is not publicly available, but it is available from the corresponding author upon reasonable request.

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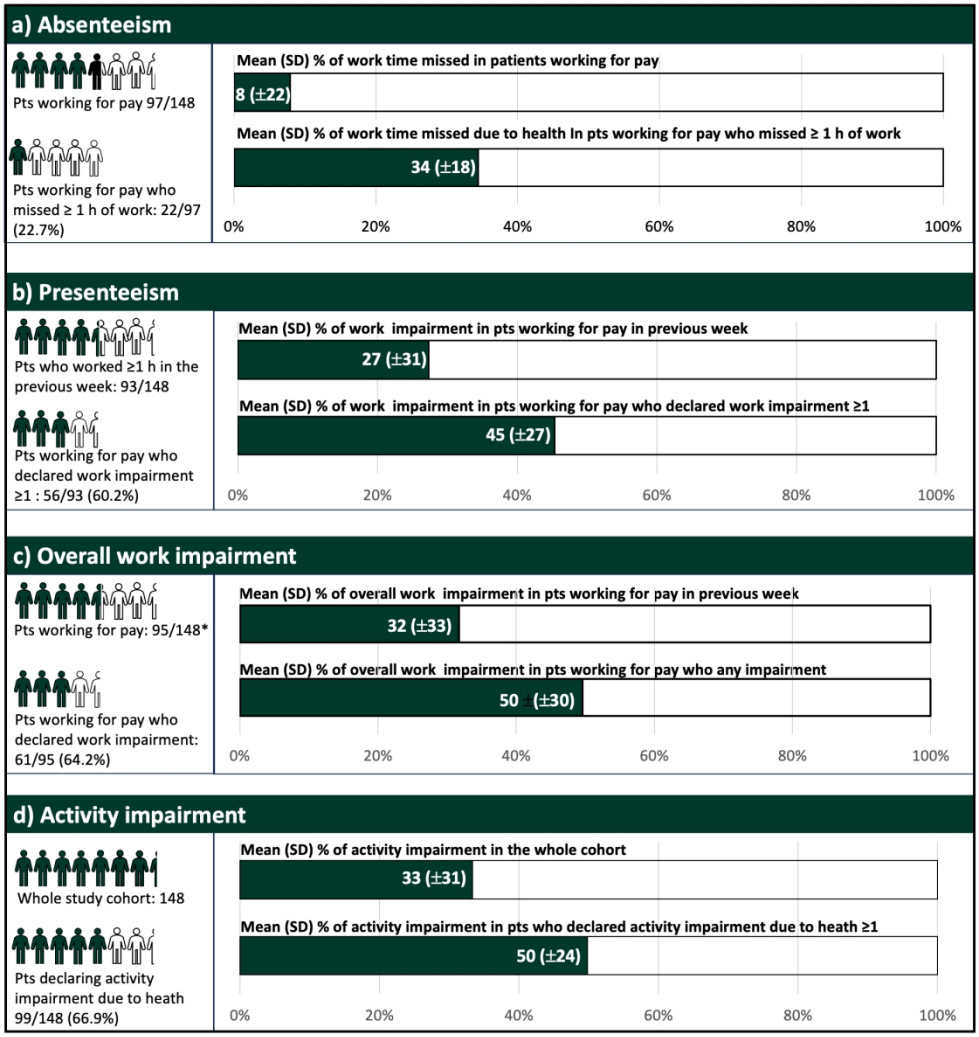
Table 1. Baseline features of the BODI sub-cohort (n = 148)

	(n=148)
Demographics	
Female gender, n (%)	72 (48.6)
Age at enrolment, mean ±SD years	46.2 ±12.1
Disease duration, mean ±SD years	13.9 ±9.9
Cumulative clinical manifestations	
Oral aphtosis, n (%)	147 (99.3)
Genital aphtosis, n (%)	111 (75.0)
Skin lesions, n (%)	114 (77.0)
Ocular manifestations, n (%)	87 (58.8)
Neurologic lesions, n (%)	29 (19.6)
Vascular lesions, n (%)	31 (20.9)
Pathergy test, n (%)	23 (15.5)
Arthritis, n (%)	96 (64.9)
Gastrointestinal manifestations, n (%)	27 (18.2)
Active clinical manifestations	
Oral aphtosis, n (%)	54 (36.5)
Genital aphtosis, n (%)	8 (5.4)
Skin lesions, n (%)	14 (9.5)
Ocular manifestations, n (%)	4 (2.7)
Neurologic lesions, n (%)	2 (1.4)
Vascular lesions, n (%)	0 (0.0)
Arthritis, n (%)	22 (14.9)
Gastrointestinal manifestation, n (%)	7 (4.7)
Ongoing treatment	
Glucocorticoid ongoing, n (%)	52 (35.1)
Conventional Immunosuppressants, n (%)	60 (40.5)
TNF inhibitors, n (%)	41 (27.7)
Disease activity	
BDCAF, mean ±SD score	3.1 ±3.2
PGA, mean ±SD cm	2.3 ±2.1
PtGA, mean ±SD cm	2.9 ±2.3
Organ damage	
BODI, mean ± SD score	1.9 ±2.1
BODI ≥1, n (%)	101 (68.2)

SD, standard deviation. BDCAF, Behçet's Disease Current Activity Form. PGA, Physician Global Assessment. PtGA, Patient Global Assessment. BODI, Behcet's syndrome overall damage index.

Figure 1. Representation of the value of absenteeism (a), presenteeism (b), overall work impairment (c), and daily activity impairment (d) in the studied cohort. In the left boxes, the proportion of the population analyzed, and the prevalence of the different outcomes were reorientated. In the right boxes, the mean (SD) value of absenteeism, presenteeism, overall work impairment, and daily activity impairment in the respective sub-cohorts.



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