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ORIGINAL RESEARCH

# Evaluation of fatigue and its correlation with quality of life index, anxiety symptoms, depression and activity of disease in patients with psoriatic arthritis

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Claudio Carneiro[1,2]
Mario Chaves[2]
Gustavo Verardino[2]
Ana Paula Frade[3]
Pedro Guimaraes Coscarelli[4]
Washington Alves Bianchi[5,6]
Marcia Ramos-e-Silva[3]
Sueli Carneiro[2,3]

[1]Health Ministry, [2]Sector of Dermatology, School of Medical Sciences and University Hospital, State University of Rio de Janeiro, [3]Sector of Dermatology, University Hospital and School of Medicine, Federal University of Rio de Janeiro, [4]General Medicine Department, University Hospital and School of Medical Sciences, State University of Rio de Janeiro, [5]Sector of Rheumatology, Santa Casa da Misericórdia, [6]University Hospital and School of Medical Sciences, State University of Rio de Janeiro, Rio de Janeiro, Brazil

**Background:** Psoriatic arthritis is associated with psychosocial morbidity and decrease in quality of life. Psychiatric comorbidity also plays an important role in the impairment of quality of life and onset of fatigue.

**Objectives:** This study aimed to assess the prevalence of fatigue in psoriatic arthritis patients and to correlate it to quality of life indexes, functional capacity, anxiety, depression and disease activity.

**Patients and methods:** This cross-sectional study was performed on outpatients with psoriatic arthritis. Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F; version 4) was used to measure fatigue; 36-Item Short Form Health Survey (SF-36) and Psoriasis Disability Index (PDI) to measure quality of life; Health Assessment Questionnaire (HAQ) to assess functional capacity; Hospital Anxiety and Depression (HAD) scale to measure anxiety and depression symptoms; Psoriasis Area and Severity Index (PASI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Clinical Disease Activity Index (CDAI) to evaluate clinical activity.

**Results:** In all, 101 patients with mean age of 50.77 years were included. The mean PDI score was 8.01; PASI score, 9.88; BASDAI score, 3.59; HAQ score, 0.85; HAD – Anxiety (HAD A) score, 7.39; HAD Depression (HAD D) score, 5.93; FACIT–Fatigue Scale (FACIT-FS) score, 38.3 and CDAI score, 2.65. FACIT-FS was statistically associated with PASI ($r_s$ –0.345, $p$<0.001), PDI ($r_s$ –0.299, $p$<0.002), HAQ ($r_s$ –0.460, $p$<0.001), HAD A ($r_s$ –0.306, $p$=0.002) and HAD D ($r_s$ –0.339, $p$<0.001). The correlations with CDAI and BASDAI were not confirmed. There was statistically significant correlation with all of the domains of SF-36 and FACIT-F (version 4).

**Conclusion:** Prevalence of fatigue was moderate to intense in <25% of patients with psoriatic arthritis. Fatigue seems to be more related to the emotional and social aspects of the disease than to joint inflammatory aspects, confirming that the disease's visibility is the most disturbing aspect for the patient and that "skin pain" is more intense than the joint pain.

**Keywords:** psoriasis, arthritis, fatigue, quality of life, anxiety, depression, questionnaires

## Introduction

Psoriasis (Ps) is a chronic inflammatory disease with worldwide distribution affecting both sexes in the proportion of 1 man:1.3 women, at any age, but more frequently in the 3rd and 4th decades of life. The predisposition seems to be genetically determined and familial occurrence is present in ~30% of cases.[1]

Psoriatic arthritis (PA) has characteristic features of joint inflammation, with edema, erythema and heat in one or more joints; Moreover, 6%–40% of patients

Correspondence: Marcia Ramos-e-Silva
Sector of Dermatology, University Hospital and School of Medicine, Federal University of Rio de Janeiro, Rua Dona Mariana 143/C-32, Rio de Janeiro 22280-020, Brazil
Email ramos.e.silva@dermato.med.br

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with Ps have arthritis.[2–7] The age for the beginning of PA is ~40 years, and patients with severe forms may have earlier manifestation.[8]

Fatigue is a frequent complaint in patients with arthritis, which they correlate to tiredness.[9,10] In humans, fatigue is more central than peripheral, as well as being more psychological than physiological and thus is very difficult to quantify.[11,12] It is the result of biochemical and physiological changes and is manifested by weakness, weariness and behavioral disturbances with reduced work capacity or lack of resistance and a subjective feeling of tiredness and discomfort.[12–16] There is no detection of actual muscle weakness in most people who complain of fatigue. The fatigued individual cannot handle complex problems and tends to be less reasonable in everyday life and to exhibit inferiority complex, anxiety and depression.[12,15,17,18]

Multiple factors accelerate the onset of fatigue, including heat, humidity and altitude, while others, such as pleasure, rhythm, motivation, knowledge of the stages of the task to be performed and fitness, delay it. Sex and age also influence the onset of fatigue.[12,17]

Almost all chronic diseases may evolve with fatigue. The differential diagnosis includes infections; anemia; neoplastic, connective tissue, endocrine, neurological, chronic kidney, chronic liver, metabolic and ionic diseases; sleep and psychiatric alterations; and many others.[19–22]

Quality-of-life (QoL) health status refers to "dimensions" that are specific and directly related to health conditions, excluding environmental factors, income, beliefs and freedom.[23–26]

The global well-being of patients and their cohabitants, who experience impairment in QoL of patients and higher levels of anxiety and depression, is markedly worsened by Ps.[27] Tezel et al[28] studied 80 patients with PA, 40 patients with Ps and 40 healthy subjects in terms of QoL and functional status and found that patients with Ps and PA had worse QoL and patients with PA had worse functional status than healthy individuals.

The severity of Ps is usually assessed only relative to the extent of the skin or joint involvement, leaving aside the assessment of fatigue, QoL and symptoms of anxiety and depression. However, Ps may provoke a negative impact as large as that of debilitating and life-threatening disorders. Such effects include stress, embarrassment, stigma and physical discomfort. Over time, there is an increasing emotional involvement of the patient to the detriment of his/her social life, decreased productivity at school or work and lower self-esteem. Patients believe that fatigue is linked to the disease activity, poor sleep, stress of joint components and lack of sense of well-being, and they consider it more important than the joint symptoms.[29,30]

The objectives of this investigation were to verify the prevalence of fatigue in patients with PA undergoing treatment at the outpatient clinics of 2 university hospitals in Rio de Janeiro, through the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) tool; to assess the disease activity, QoL, functional capacity and symptoms of depression and anxiety in these patients and, finally, to correlate fatigue with the QoL index, functional capacity, symptoms anxiety and depression, as well as disease activity.

## Patients and methods

This was a cross-sectional observational clinical–epidemiological study.[31] The research project was approved by the ethical committees of both hospitals: Clementino Fraga Filho University Hospital (Federal University of Rio de Janeiro – UFRJ) and Pedro Ernesto University Hospital (State University of Rio de Janeiro – UERJ).

### Patients

Patients of both sexes (n=101), aged ≥18 years, with clinical diagnoses based on the 2006 *Classification Criteria for Psoriatic Arthritis* (CASPAR)[32] were examined. All patients provided signed informed consent. They were from the Sector of Dermatology (Cutaneous–Articular Diseases Out-Patient Clinic) of the Clementino Fraga Filho University Hospital (Federal University of Rio de Janeiro) and Sector of Rheumatology (Spondiloarthritis Out-Patient Clinic) of the Pedro Ernesto University Hospital (State University of Rio de Janeiro). Exclusion criteria were diabetes, liver or kidney failure, hypothyroidism or untreated adrenal insufficiency, neurological diseases from constant muscle activity, myopathy, anemia (hematocrit <30%) and chronic infections, as well as use of medications such as diuretics, beta-blockers, methyldopa and barbiturates. Hospitalized or home-in-bed patients were also excluded.

### Methods

Patients who fulfilled the CASPAR were interviewed, and they answered the questionnaires, for which permission for use was obtained from the authors by email. After a brief explanation by one of the health care team members, the following protocols were filled out: 36-Item Short Form Health Survey (SF-36),[33] Psoriasis Disability Index (PDI),[30] Hospital Anxiety and Depression (HAD) scale,[34] FACIT-F, FACIT–Fatigue Scale (FACIT-FS)[35] and Health Assessment

Questionnaire (HAQ).[36] Disease activity was measured with Psoriasis Area and Severity Index (PASI),[37] Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[38] and Clinical Disease Activity Index (CDAI).[39]

## Statistical evaluation

The 2 × 2 tables were analyzed with Fisher's exact test. In the remaining contingency tables, the $\chi^2$ test was used. In the correlation analysis, the Pearson correlation coefficient *r* was used. The level of statistical significance was set at 0.05. All analyses were performed with the R software, version 2.11, free and open source code.

# Results

## Population studied

Three hundred patients with Ps from the Sector of Dermatology of the Clementino Fraga Filho University Hospital, UFRJ (Cutaneous–Articular Diseases Out-Patient Clinic) and 150 patients with spondyloarthritis from the Sector of Rheumatology of the Pedro Ernesto Hospital, UERJ (Spondyloarthritis Out-Patient Clinic) were evaluated, and of them, 101 fulfilled the inclusion criteria, with the following characteristics:

Sex: 57 men (56.4%) and 44 women (43.6%)

Color: 61 Caucasian, 33 mixed and 7 black

Average age: 50.77 years (sd =0.48); minimum: 23 years; maximum: 79 years

## Articular disease

The articular disease was clinically and/or radiologically diagnosed and showed the distribution presented in Table 1.

## QoL, fatigue, functional capacity and disease activity

The SF-36 tool with 8 domains is presented in Table 2. All domains (FC, functional capacity; PAL, physical aspects limitation; GHS, general health status; SA, social aspects; EA, emotional aspects; VIT, vitality) ranged from 0 to 100, except PAIN, whose minimum value was 10, and mental health (MH), whose minimum value was 24.

The intermediary values show that all SF-36 domains were impaired by the disease.

**Table 1** Distribution of articular involvement

| Articular involvement | Women/men | White | Mixed | Black |
|---|---|---|---|---|
| Peripheral | 26/22 | 25 | 21 | 2 |
| Axial | 1/13 | 10 | 3 | 1 |
| Both | 17/22 | 26 | 9 | 4 |

**Table 2** Distribution of SF-36 components

| SF-36 domains | Median | Mean |
|---|---|---|
| FC | 60 | 59.52 |
| PAL | 50 | 51.04 |
| PAIN | 42 | 52.59 |
| GHS | 62 | 59.81 |
| SA | 62.50 | 63.72 |
| MH | 68 | 65.71 |
| EA | 97 | 66.77 |
| VIT | 60 | 58.5 |

**Note:** PAIN indicates the pain domain of SF-36.
**Abbreviations:** SF-36, 36-Item Short Form Health Survey; FC, functional capacity; PAL, physical aspects limitation; GHS, general health status; SA, social aspects; MH, mental health; EA, emotional aspects; VIT, vitality.

There are 4 domains of FACIT-F, as seen in Table 3 (PW, physical well-being; S/F W, social and family well-being; EW, emotional well-being; FunW, functional well-being and a Fatigue Scale). There are specific scores that add some domains, such as TOI (PW + FunW + Fatigue Scale), G (PW + S/F W + EW + FunW) and F (PW + S/F W + EW + FunW + Fatigue Scale).

The FACIT-F domains showed alterations, as did the SF-36 that measures the same variables. The sum of scores (TOI, F and G) also showed alterations.

Fatigue was intense to moderate in the 1st quartile (25 patients), as seen in Figure 1.

FACIT Scale, PASI, PDI, BASDAI, HAQ, HAD A, HAD D and CDAI scores showed minimum and maximum values as distributed in Table 4, which shows the variation of the scores found for fatigue, disease activity, QoL, functional capacity as well as the symptoms of anxiety and depression.

The correlation was strong between the FACIT-FS and the skin disease activity rates, as assessed by PASI; QoL assessed by PDI; and anxiety and depression assessed by HAD. However, the correlations with the peripheral and axial joint disease activity indexes, as assessed by the BASDAI and the CDAI, were not confirmed. Figures 2 and 3 illustrate these findings.

**Table 3** Distribution of FACIT-F (version 4) components

| Domain | Minimum | Maximum | Median | Mean |
|---|---|---|---|---|
| PW | 1 | 28 | 21.00 | 27.00 |
| S/F W | 3 | 28 | 20.00 | 20.71 |
| EW | 3 | 24 | 17.00 | 16.82 |
| FunW | 0 | 28 | 18.27 | 18.00 |
| TOI | 2 | 107 | 74.00 | 75.70 |
| G | 25 | 107 | 73.30 | 76.18 |
| F | 25 | 159 | 113.5 | 113.59 |

**Notes:** TOI, PW + FunW + FACIT F; G, PW + S/F W + EW + FunW; F, PW + S/F W + EW + FunW + FACIT F.
**Abbreviations:** FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; PW, physical well-being; S/F W, social and family well-being; EW, emotional well-being; FunW, functional well-being.

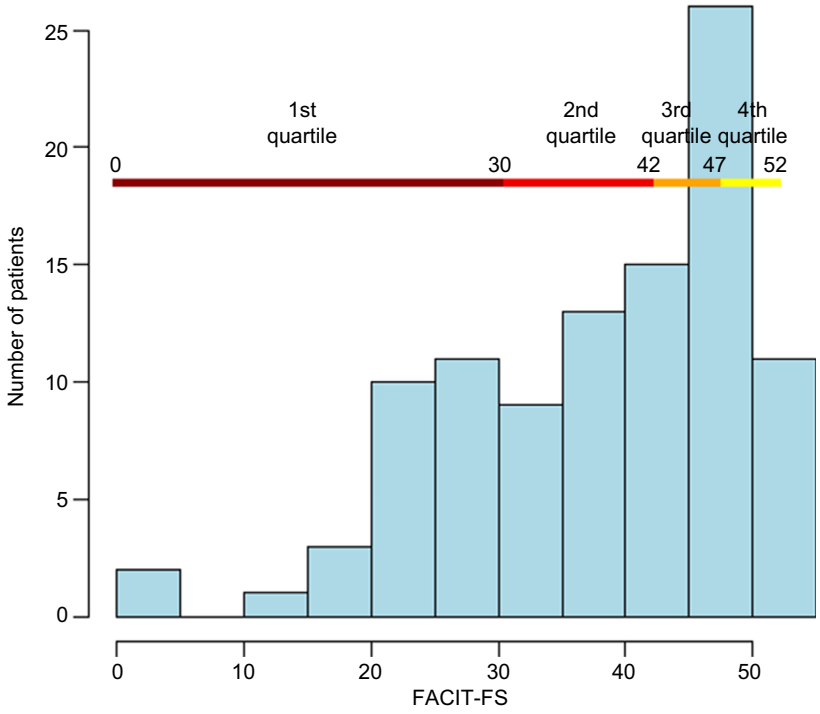



**Figure 1** Distribution of FACIT-FS scores.
**Abbreviation:** FACIT-FS, Functional Assessment of Chronic Illness Therapy–Fatigue Scale.

**Table 4** Distribution of FACIT-FS, PASI, PDI, BASDAI, HAQ, HAD A/D and CDAI domain values

| Instrument | Minimum | Maximum | Median | Mean |
|---|---|---|---|---|
| FACIT-FS | 0 | 52 | 42 | 38.3 |
| PASI | 0 | 39.9 | 8 | 9.88 |
| PDI | 0 | 35 | 5 | 8.01 |
| BASDAI | 0 | 9.25 | 3.2 | 3.59 |
| HAQ | 0 | 2.90 | 0.88 | 0.85 |
| HAD A | 0 | 21 | 7 | 7.39 |
| HAD D | 0 | 20 | 6 | 5.93 |
| CDAI | 2 | 58 | 24 | 24.65 |

**Abbreviations:** FACIT-FS, Functional Assessment of Chronic Illness Therapy–Fatigue Scale; PASI, Psoriasis Area and Severity Index; PDI, Psoriasis Disability Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAQ, Health Assessment Questionnaire; HAD A/D, Hospital Anxiety and Depression scale – Anxiety/Depression; CDAI, Clinical Disease Activity Index.

The correlation was strong between FACIT-F and the different domains of SF-36 that included not only physical and functional aspects but also emotional, social and mental health, ranging below 0.001.

Fatigue Scale scores were correlated with FACIT-F domains, which included not only physical and functional aspects, but also those that assessed emotional and social aspects. There were no correlations with TOI and F score sums because both contain the FACIT Scale.

## Discussion

Ps has a high worldwide prevalence and a broad spectrum of cutaneous and articular manifestations, with a negative impact on the QoL, function, indexes of anxiety and depression as well as increased sensation of fatigue, especially in the presence of associated arthritis, and may be associated with decreased survival.[40]

Lomholt[41] suggested that the earlier the disease starts in a population, the more the environmental factors involved in its onset are relevant. The low PASI, PDI and fatigue scores in our patients can be credited to the sunny climate of the city of Rio de Janeiro and the daily habits of wearing less clothing and more sun exposure of its inhabitants, and the fact that Rio de Janeiro is one of the happiest cities in the world.[42,43]

There are no specific indicators to assess the disease activity in PA, or they are still in the process of validation. The tools deployed nowadays for assessing the disease have been insufficiently validated or are borrowed from rheumatoid arthritis (RA). We decided to use the CDAI, unlike other indexes used in RA, which does not include any measure in response to the acute phase response (APR) in its formula. In cases of PA, the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) do not assume high values and often bear no relation with the intensity of the inflammation. The CDAI designed for RA may therefore be used in PA and other arthritis models.[39]

At the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) meetings,[44] the possibility of using an already existing measure to evaluate PA or the need to create a new one specific to the disease was discussed

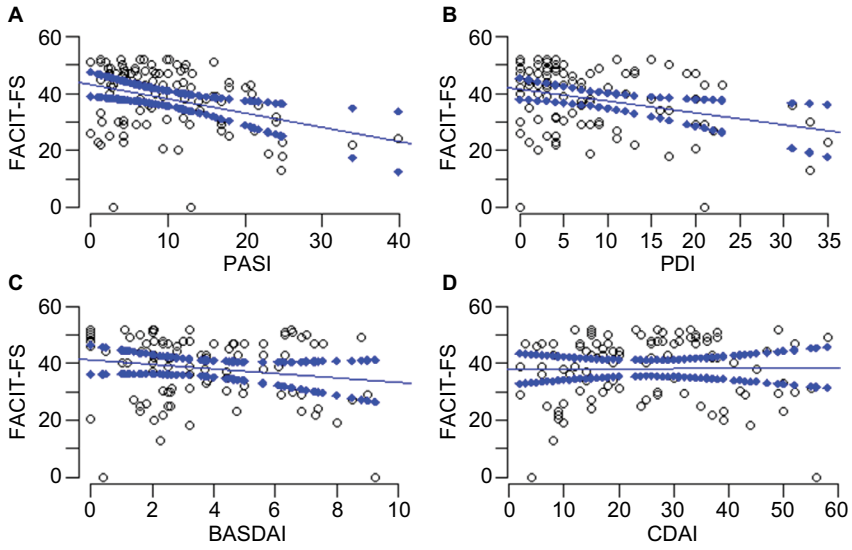



**Figure 2** Correlation between FACIT-FS scores and (**A**) PASI, (**B**) PDI, (**C**) BASDAI and (**D**) CDAI scales.
**Note:** Scatter plots and adjustment curves of 95% CI (confidence interval) are shown.
**Abbreviations:** FACIT-FS, Functional Assessment of Chronic Illness Therapy– Fatigue Scale; PASI, Psoriasis Area and Severity Index; PDI, Psoriasis Disability Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CDAI, Clinical Disease Activity Index.

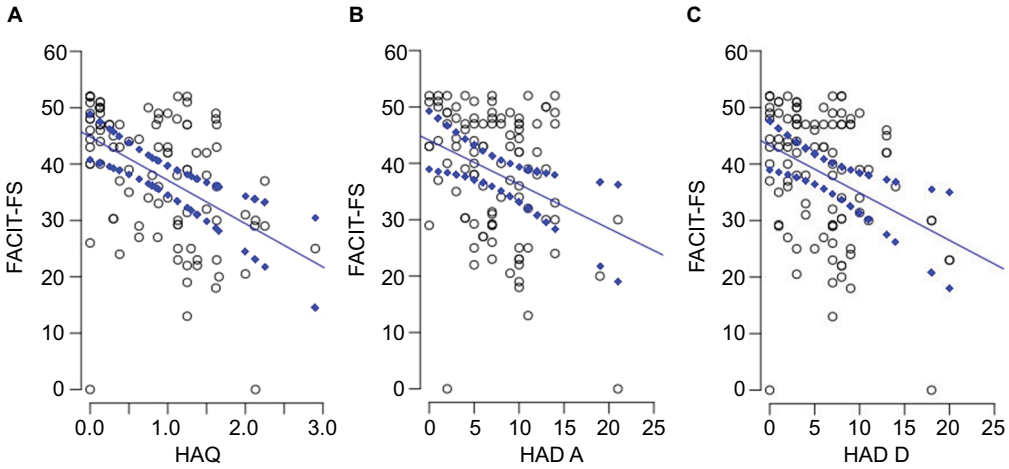



**Figure 3** Correlation between FACIT-FS scores and (**A**) HAQ, (**B**) HAD A and (**C**) HAD D scales.
**Note:** Scatter plots and adjustment curves of 95% CI (confidence interval) are shown.
**Abbreviations:** FACIT-FS, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; HAQ, Health Assessment Questionnaire; HAD A/D, Hospital Anxiety and Depression scale – Anxiety/Depression.

several times and their advantages and disadvantages were analyzed.[45]

Gupta and Gupta [46] reported that Ps has a greater impact on the QoL of patients aged between 18 and 45 years, and that men suffer a higher degree of work-related stress due to the disease. These authors did not find any differences between sexes in terms of the disease's severity.

Sampogna et al,[47] in their assessment of hospitalized patients, found that women aged >65 years had a greater reduction in QoL related to Ps. In this study, only patients with arthritis aged >18 years were included, and the PASI average was 9.88 and the PDI average was 8.01, showing that even in this population, the majority of patients showed an impairment that can be considered mild to moderate, corroborating the influence of environmental factors, which was also observed by one of the authors (unpublished data).[48]

Most studies consider stress a factor significantly related to the worsening of the disease. Each population has specific psychological characteristics. Thus, the manner in which coastal city-dwelling Brazilians deal with stress and how it influences the disease is a relevant topic in the study of Ps.

Various types of questionnaires have been developed in an attempt to assess patients' QoL, including questions about physical and mental health, as well as aspects related to their family, friends and social life. These questionnaires can be generic or specific to dermatology diseases and these provide scientific and systematic grounds to measure what matters to the patient.[49]

The variation between the QoL questionnaires is often related to the degree to which they emphasize objective dimensions compared to subjective ones, the extent to which the various areas are covered and the format of questions rather than differences in the definition of QoL.[49,50]

For this study, the PDI was chosen for including some detailed domains, such as personal relationships, leisure and daily activities, whether at school, at work or in general. Moreover, Japiassu, in 2008,[48] noted that PDI and Dermatology Life Quality Index (DLQI), widely used for all dermatoses, are reliable and equivalent to evaluate the QoL of Ps patients with or without arthritis.

Studies on fatigue in RA have shown that patients consider their fatigue frustrating and exhausting and that it is much more related to pain intensity, depressed mood and nonrestorative sleep than to the inflammation itself and anemia.[9,51–53] For many patients, fatigue is not a disorder, but something expected and normal in their daily routine.[54,55]

Pollard et al[51] concluded that disease activity does not play any role in the level of fatigue and the relation between inflammation and fatigue is not as strong as generally assumed. Psychosocial factors may be important in the perpetuation of fatigue, and some of them may make certain patients more prone to fatigue.

Treharne et al[55] stated that psychological factors and depression are major contributors to fatigue, but not the only ones. The pain, the disease activity and the painful joint count were moderately associated, while swollen joints, anemia, ESR and PCR were not. Skin diseases are known to have deleterious effects on the QoL of patients and Ps, considered by many as a psychodermatosis amid its multicausality, presents the psychosocial factor to a relevant extent. Indeed, social and psychological factors are codeterminants of the health–disease process, in a biopsychosocial model, wherein diseases are the result of several factors. The contribution of psychosocial factors varies from disease to disease, from person to person and between worsening episodes in the same person.

It has already been shown that the patients' vision of Ps is not associated with the severity of the case, suggesting that they respond psychologically more to their own view than to the actual severity of the disease. It explains why it is sometimes not possible to associate the impact of Ps with the severity of the condition, or why this ratio is weak.[56]

When the domains of QoL are stratified, the most affected in Ps are personal relationships and daily activities, reflecting the stigmatizing burden in patients' everyday life, particularly in relationships. It is therefore important to evaluate the Ps patient's perception regarding their health, disability and their QoL, as well as how this perception is associated with the perception of pain and fatigue.

The negative impact of Ps on different QoL domains is comparable to, or even greater than that of, other potentially fatal chronic diseases.[57] Patients with severe Ps associated with diabetes, asthma or bronchitis would rather have the underlying disease than the skin disease.[25] Many patients, when comparing the involvement of the joint with that of the skin, literally say that the skin bothers them much more than the pain, inflammation and joint deformity.

Studies in patients with Ps show that 3 out of 4 patients avoid sporting or swimming activities because of the disease, one-third of them are inhibited in their sexual relationships and the disease influences career choices in 25%.[58,59]

Hughes et al [60] were the first to demonstrate that dermatological patients, whether outpatients or hospitalized, have higher prevalence of psychiatric disorders than the general population. Since then, several studies have been published reporting a prevalence ranging from 14% to 70%,[61–64] although causal inferences cannot be made due to their sectional designs. A prospective study with dermatological patients without psychiatric morbidity at the first visit showed an incidence of psychiatric disorders, after 1 month, by 7.6%, with even higher percentages in patients with unsatisfactory treatment results.[65] The risk of developing a psychiatric disorder was 3 times higher in patients who did not get better with treatment.[64] Magin et al[66] demonstrated, in a longitudinal study, evidence that stress and depression, but not anxiety, may play a role in the multifactor etiology of skin diseases. Longitudinal studies are therefore needed to define the correct direction of this association.

Although studies conducted in Western populations have shown that the prevalence of nonpsychotic mental disorders ranges from 7% to 26%, with an average of 17% (12.5% in men and 20% in women), studies show that, in Brazil, this rate can be much higher, ranging from one-third to 50% of patients.[67] The average PDI value was 8.4, higher than the value of 7.6 found by Japiassu.[48] Such values correlated with fatigue in a statistically significant way.

Although the association between the disease and the presence of symptoms of anxiety and depression was high in the study due to its sectional design, it was not possible to establish the correct causal relationship between both of them and fatigue, with which it was statistically significantly correlated.

Using PDI with HAD and fatigue represents an interesting study strategy, because both deal with issues linked to emotional aspects of the life of patients who have a skin disease.

Minnock et al[68] measured fatigue as a sensitive and independent pattern in PA patients treated with anti-tumor necrosis factor (TNF), using a numerical scale from 0 to 10. Fatigue levels were 5.6 (2.3) and 3.6 (2.2) ($p$=0.001) at the beginning and 3 months later, respectively, and it was found that fatigue was an independent and sensitive measure to assess changes in patients with PA, when compared with HAQ, pain and CRP.

Gladman et al[69] assessed the effects of 40 mg of subcutaneous adalimumab every 14 days in terms of functional impairment, QoL, fatigue and pain in patients with PA compared to placebo. The same questionnaires were used and they concluded that the group treated with anti-TNF experienced reductions in their functional limitations, fatigue and pain, along with an improved QoL.

Fatigue was moderate to severe in a quarter of patients, less prevalent than seen in RA,[51–53] and correlated with the disease activity and not the cutaneous articular disease, confirming the findings that the visibility of the disease is highly relevant to patients and that the "skin pain" and the "soul pain" are much more intense than the pain and joint inflammation.[56]

## Conclusion

Fatigue was prevalent in patients with PA monitored in the Cutaneous–Articular Diseases Out-Patient Clinic of HUCFF/UFRJ and in the Spondyloarthritis Out-Patient Clinic of HUPE/UERJ. It was intense to moderate in a quarter of patients. The PASI, BASDAI and CDAI indexes were satisfactory in the evaluation of disease activity and were consistent with mild-to-moderate disease intensity in most patients. The HAQ was able to assess patients' functional capacity, showing that the average inability ranged from mild to moderate, while SF-36, PDI and FACIT-F were able to assess the QoL in its many aspects, showing greater impairment in personal relationships, emotional aspects and daily activities. The fatigue assessed by the FACIT-FS statistically significant correlated the indexes of QoL and the symptoms of anxiety and depression with the disease activity assessed by PASI. There was no correlation, however, with CDAI nor with BASDAI, which measure the articular and axial disease activity. The "skin pain" seems to be more intense than the joint pain.

### Final considerations

The study of fatigue in PA is intriguing and leads to several considerations: Is depression a cause or a consequence of the disease and of its severity? Is there a distinct pattern of response to stress in patients with Ps? How to assess it? What is the real influence of environmental factors on fatigue? Is the disease's visibility the only factor valued by the patient? What is the magnitude of the "skin pain"?

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## Disclosure

The authors report no conflicts of interest in this work.

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