Association between Comorbidities and Quality of Life in Psoriatic Arthritis: Results from a Multicentric Cross-sectional Study (PSAQUAL study)

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The study protocol was approved by the local Institutional Review Board (reference 2018-A00449-46), and the study procedures complied with the ethical standards of the relevant institutional and national Human Experimentation Ethics Committees (reference CPP 3590-NI), and the Helsinki Declaration of 1975, as revised in 2000. All patients provided written informed consent.

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WB participated in the design of the study and helped to draft the manuscript. XD participated in the design of the study and helped to draft the manuscript. EH participated in the design of the study and helped to draft the manuscript. PP participated in the design of the study and helped to draft the manuscript. VD participated in the design of the study, helped to draft the manuscript and performed the statistical analysis. RMF participated in the design of the study and helped to draft the manuscript. JP conceived of the study, participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Objective In psoriatic arthritis (PsA), comorbidities add to the burden of disease, which may lead to poorer quality of life. The purpose of this study was to evaluate the relationship between comorbidities and quality of life (QoL).

Methods Patients from a multicentric, cross-sectional study on comorbidities in PsA were included in the analysis. Data on comorbidities were collected and were subsequently used to compute the modified Rheumatic Disease Comorbidity Index (mRDCI). The Medical Outcomes Study Short Form-36 (SF-36) physical (PCS) and mental component (MCS) summary scales were used to assess QoL.

Results In total, 124 recruited patients fulfilled the CASPAR criteria: 62.1% were male; mean age and mean disease duration were 52.6 ± 12.6 and 11.3 ± 9.6 respectively. The number of comorbid conditions was 2.0 ± 1.3, with 30.6% of the sample having a current or past history of 3 or more comorbidities. In the multivariate linear regression analysis, only anxiety remained significantly related to mental health ($p<0.0001$). Anxiety alone accounted for 28.7% of the variance in MCS scores. Moreover, MCS was also significantly associated with the mRDCI score, which explained 4.9% of the variance in MCS (β=-1.56 (0.64), R^2=0.049, p=0.0167). In contrast, PCS was not significantly associated either with type or number of comorbidities.

Conclusion In this study, the type of comorbidity appeared to have a greater impact than the number of comorbidities. Indeed, anxiety in PsA was independently associated with QoL and would thus be an important factor to take into account in daily clinical practice.

Significance & Innovations

Type of comorbidity appeared to have a greater impact than the number of comorbidities on quality of life in PsA.

Anxiety in PsA was independently associated with quality of life.

Screening for, rating the severity of, and managing anxiety could contribute to improving quality of life in PsA.

INTRODUCTION

Psoriatic arthritis (PsA) is a member of the spondyloarthritis family (1). The protean cutaneous and rheumatic manifestations result in a variety of presentations. Since the development of classification criteria by Moll and Wright in 1973 (2), five patterns of PsA have been individualized: polyarthritis, oligo-polyarthritis, distal interphalangeal arthropathy, predominantly axial disease, and arthritis mutilans (1,3). Among the many classification schemes proposed for PsA, the most recent is the CASPAR system, which was developed in 2006 by a panel of international experts (4,5). A multidisciplinary treatment strategy is mandatory and must address not only the rheumatic manifestations, but also the skin disease (6–9).

The COMOSPA study reveals a high prevalence of related comorbidities in spondyloarthritis (SpA), and their assessment and management is a real concern (10,11). Psoriatic arthritis is also associated with multiple comorbid conditions including cardiovascular (CV) comorbidities (12–14) and other PsA-related comorbidities such as diabetes, anxiety, fatigue, smoking, alcohol use, obesity or overweight, depression and osteoporosis (1,14–19). Comorbidities and their impact on disease outcomes are generally well-described for rheumatoid arthritis (RA), but less so for PsA (15,20–22). However, in a cohort of Danish patients with PsA (DANBIO), the presence of comorbidities was associated with higher baseline disease activity, shorter TNFi persistence, and reduced clinical response rates (23). Moreover, obesity was associated with a lower probability of achieving sustained minimal disease activity (MDA) among patients with PsA (24).

Furthermore, comorbidities add to the burden of disease and may lead to poorer quality of life (QoL), which is also an outcome of great interest. A few studies have shown associations between individual comorbidities and QoL in patients with SpA (25) or particularly with PsA. In a study conducted by Husted *et al.* (26), the authors found that fibromyalgia (FM), neurological disorders, and obesity were most strongly associated with decreased physical Health (PCS), whereas FM and depression/anxiety disorders were most strongly associated with decreased mental health (MCS). As such, there is still a lack of data on the relationship between comorbidities and outcomes in PsA.

The purpose of this study was to assess the relationship between comorbidities and QoL in patients with PsA in a well-phenotyped cohort from Les Hauts-de-France region of France. We hypothesized that the effect of comorbidity on QoL in PsA was more closely related to type of comorbidity than number of comorbidities.

PATIENTS AND METHODS

Study design and patient recruitment

This is a multicenter, cross-sectional observational study with 3 participating centers (Lille University Hospital, Lille Catholic Hospitals and Valenciennes Hospital). PsA patients admitted in conventional hospital units, day hospitalization or in outpatient clinics were invited to participate. Consecutive patients (ages ≥18 years) with a clinical diagnosis of peripheral PsA (polyarthritis and oligo-polyarthritis patterns) were included in this study provided they were able to understand and complete the questionnaires. For this study, analyses were restricted to patients fulfilling the CASPAR criteria for PsA (4). Exclusion criteria were lack of understanding of French, pregnancy or breastfeeding, severe cognitive disorders, guardianship, lack of social welfare access.

The study protocol was approved by the local Institutional Review Board (reference 2018-A00449-46), and the study procedures complied with the ethical standards of the relevant institutional and national Human Experimentation Ethics Committees (reference CPP 3590-NI), and the Helsinki Declaration of 1975, as revised in 2000. All patients provided written informed consent.

Data collection

Outcome measure

In this study, the outcome of interest was measured using the Short Form (36) Health Survey (SF-36) questionnaire as a generic measure of QoL (27). Specifically, the physical and mental health component scales (PCS and MCS) were used. We used the revised version of the SF-36v1 questionnaire (amendment QMO46180, license agreement amended QMO44954). Both scales are linear combinations of the eight SF-36 subscales, with the PCS heavily weighting the physical function, bodily pain, and role disabilities due to physical limitations subscales, and the MCS heavily weighting the mental health, social function, and role disabilities-emotional limitations subscales. Scores below 50 reflected below-average function. Very low PCS scores reflected severe bodily pain and substantial limitations in self-care, physical activities, and role performance. Very low MCS scores indicated frequent psychological distress and role disability due to emotional problems.

Comorbidities

Data on comorbidities were based on both self- and physician-report, as per the self-administered questionnaire developed by Pouplin *et al.* (28). Each patient's electronic medical file was systematically checked by the investigator (WB) to complete and rectify the self-reported data. For each patient, the type and the number of comorbidities (range 0-9) were collected. Types of comorbidity included cardiovascular disease, malignancy, diabetes mellitus, excess weight, pulmonary problems, depression, anxiety, fibromyalgia and osteoporosis.

Cardiovascular disease included history of ischemic disease (myocardial infarction and stroke), angina, stent, carotid atheromatous plaques, and peripheral vascular disease. Malignancy included history of carcinoma of the colon, skin (i.e., melanoma and basocellular carcinoma), breast and cervix (for women), prostate (for men), lymphoma (sought systematically), and others if reported by the patients. Diabetes mellitus included history of diabetes mellitus obtained through self- and physician-report. Data on current medications commonly used for patients with diabetes mellitus were collected. Excess weight included overweight (BMI of 25-29.9 kg/m²) and obesity (BMI $\geq$ 30 kg/m²). Pulmonary problems included history of chronic obstructive pulmonary disease (COPD) and asthma. Depression, anxiety, and fibromyalgia included history of those diseases obtained through self- and physician-report. We also collected data on current medications commonly used for patients suffering from depression and anxiety. Osteoporosis included history of osteoporosis (defined as a T-score of less than -2.5 at any site), non-traumatic vertebral/peripheral fractures, or anti-osteoporotic agent (except vitamin D and calcium).

Information on self- and physician-reported past and current comorbidities was subsequently used to compute the modified Rheumatic Disease Comorbidity Index (mRDCI) to reflect comorbidity burden (29). The mRDCI score ranges from 0 to 12 and covers lung diseases, cardiovascular disease (myocardial infarction, stroke or other cardiovascular disease), hypertension, ulcer or other gastrointestinal disorders (liver problem, gall bladder problem, and other stomach problem), diabetes mellitus, fracture, depression, malignancy, kidney disease (eGFR <60 ml/min/1.73m²), and obesity (BMI>30 kg/m² or BMI>35 kg/m²). Moreover, the Charlson Comorbidity Index (CCI) was computed for each patient. The CCI score ranges from 1 to 42 and covers 19 weighted comorbid conditions, with the conditions and their weightings based on mortality risk (30).

Other independent variables

Other variables of interest potentially influencing the relationship between comorbidities and QoL, aside from age and sex, were sociodemographic factors such as educational status (primary and secondary education vs. university education), socio-professional category (in active employment vs. others), marital status (married vs. others), disease duration, and measures of disease activity such as the Disease Activity Score (DAS28-CRP) and psoriasis area and severity index (PASI).

We collected data on HLA–B27 status, smoking status (current, past, and never), and presence of extra-articular manifestations such as uveitis and inflammatory bowel disease (IBD). Data on current use of corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs), as well as current use of conventional synthetic and biologic disease-modifying anti-rheumatic drugs (csDMARDs and bDMARDs) were also collected.

Data analysis

Continuous variables were expressed as mean (standard deviation) and median values. Categorical variables were expressed as frequencies and percentages. Normality of distributions was assessed using histograms and the Shapiro-Wilk test.

Associations between each set of QoL scores (PCS and MCS) and predetermined confounding factors (sex, age, marital status, disease duration, educational status, socio-professional category, DAS28-CRP and PASI) were investigated in univariate analysis by calculating Pearson's correlation coefficient for continuous confounding factors (or Spearman's rank correlation for non-Gaussian variables), or using the Student t test (or Wilcoxon unpaired test for non-Gaussian variables) for categorical confounding factors.

Associations between each set of QoL scores and comorbidities (individual comorbidities, number of comorbidities, mRDCI and Charlson scores) were investigated using multiple linear regression models adjusted for predetermined confounding factors (regardless of their univariate associations). Finally, a multivariate linear regression analysis of the individual comorbidities associated with QoL scores in the confounding-factors adjusted model ($p<0.20$) was performed. The collinearity between the variables included in the multivariate models was assessed by calculating the variance inflation factor (VIF) and the normality of model residuals was checked. Effect sizes for comorbidity variables were expressed as regression coefficients and partial-r squared values.

Statistical testing was performed at the two-tailed α level of 0.05. All statistical analyses were

performed using the SAS software (version 9.4).

RESULTS

Patient characteristics

Table 1 shows patients' sociodemographic and disease characteristics. The study included a group of 124 PsA patients who were predominantly male (62.1%) and Caucasian (nearly 100%). Age (mean ± SD, median) and disease duration (mean ± SD, median) were 52.6 ± 12.6, 54 years, and 11.3 ± 9.6, 10 years respectively. DAS28-CRP (mean ± SD, median) was 2.7 ± 1.1, 2.5 and nearly 55% of the patients had a DAS28-CRP score ≤ 2.6. The PASI score (mean ± SD, median) was 2.9 ± 5.4, 0.9, with no skin involvement (PASI=0) in 46 patients (37.1%). Seventy-one percent (71%) of the patients were being treated with bDMARDs (mainly TNF inhibitors).

The number of comorbid conditions (mean ± SD, median), on a scale from 0 to 9, was 2.0 ± 1.3, 2.0 (range 0–6), with 30.6% of the sample having a current or past history of 3 or more comorbidities. Supplementary Figure 1 shows the prevalence of the nine main comorbidities that were analyzed, while supplementary Figure 2 shows the prevalence of all comorbidities. The most frequent comorbidities were anxiety (44.4%), overweight (41.1%), hypertension (34.7%), depression (29.0%), obesity (29.0%), dyslipidemia (26.6%), diabetes mellitus (12.9%) and osteoporosis (11.3%). Global prevalences of myocardial infarction and stroke in the study population were 8.1% and 7.3%, respectively. Global prevalences of asthma and COPD were 7.3% and 2.4%, respectively.

Table 2 shows PCS and MCS scores on the SF-36 questionnaire. PCS and MCS values (mean ± SD, median) were 41.2 ± 9.7, 40.8 and 43.2 ± 12.4, 47.0 respectively. The most vulnerable sections were General health perception (47.2 ± 20.2, 46.0), Vitality (43.6 ± 20.6, 45.0), Role limitations due to physical health problems (48.4 ± 40.9, 50.0), and Bodily pain (48.9 ± 26.2, 51.0).

Relationships between confounding factors (sociodemographic variables and disease activity) and patient-reported physical and mental quality of life

Table 3a shows that many variables were significantly associated with physical health, as measured by the PCS. Males and patients in work were more likely to report higher PCS scores (or better physical health). Indeed, patients in work reported a better physical QoL than patients without a professional activity (mean ± SD, median: 45.1 ± 8.5, 44.8 vs. 38.1 ± 9.5,

37.9, p<0.0001). Higher disease activity (DAS28-CRP) was associated with lower levels of physical health (or lower PCS scores). DAS28-CRP was associated with level of physical function (r=-0.491, p<0.0001), whereas no correlation was found with PASI or disease duration. Table 3b shows that only one variable, DAS28-CRP, was significantly associated with MCS (r=-0.234, p=0.009), but the r value was very low suggesting that this is a poor correlation.

Association between comorbidities and quality of life

Table 4 shows the results of univariate linear regression analysis of physical and mental health on type of comorbid condition, adjusted for relevant confounders. Fibromyalgia was not evaluated due to its low prevalence (1.6%). The other 5 comorbid conditions – cardiovascular disease, anxiety, depression, respiratory disease, and cancer – were significantly associated (p<0.05) with lower levels of mental health (MCS). Based on the R^2 values, anxiety and depression were the most strongly associated with level of mental health (R^2 = 28.7% and 12.4%, respectively). Physical health (PCS) was not significantly associated with any comorbidity after adjustment for confounding factors, although there was a tendency for excess weight (β=-2.64 (1.56), R^2=0.024, p=0.09).

Table 5 shows the results of multivariate linear regression analysis of mental health on type of comorbid condition, adjusted for relevant confounders. Anxiety was strongly associated with level of mental health and accounted for 19.4% of the variance in MCS scores (β=-10.81 (2.10), R^2=0.194, p<0.0001), whereas cardiovascular disease, malignancy, depression, and pulmonary disease were no longer associated with level of mental health.

Table 6 shows the results of univariate linear regression analysis of physical and mental health on number of comorbid conditions, adjusted for relevant confounders. Number of comorbidities (range 0–6) or mRDCI score (range 0-8) accounted for 14% (β=-3.68 (0.85), R^2=0.140, p<0.0001) and 4.9% (β=-1.56 (0.64), R^2=0.049, p=0.0167) of the variance in MCS scores, respectively. In contrast, PCS was not associated with number of comorbidities, whatever the score used.

We analyzed the univariate association of the Physical health Component Scale (PCS) with the following variables: smoking, types of psoriatic arthritis, presence of extra articular manifestations (inflammatory bowel disease, uveitis), current enthesitis, current dactylitis and current treatment (bDMARDs and corticosteroid). We included factors associated with

p<0.20 (in addition to predefined confounding factors) in multivariate analyses. Similarly, we performed the same analyses for the Mental health Component Scale (MCS). All results were unchanged (data not shown)

DISCUSSION

Major findings

To the best of our knowledge, this is one of the first studies to assess the added burden of comorbidity on QoL in PsA. As expected, the prevalence of comorbidity was relatively high in our multicentric cohort of 124 patients, with 30.6% having 3 or more comorbid conditions. After adjustment for disease-related and sociodemographic factors, we were able to demonstrate that the added effect of comorbidity on patient-reported mental health in PsA was more closely related to type of comorbidity – and especially anxiety – than number of comorbidities. Moreover, no association was found between patient-reported physical health and the type or number of comorbid conditions after adjustment for those confounding factors.

Comparison with other studies

Patients with PsA have more comorbidities than the general population (12,13). In our study, the most prevalent comorbidities were excess weight (overweight/obesity, 70.2%), anxiety (44.4%), and depression (29%). Overweight and obesity are classically reported to be frequent in patients with PsA (15,19)**.** Patients with PsA have also a high risk of depression and/or anxiety (18,26), which appears to be greater than for patients with psoriasis alone (31)**.**

Cardiovascular disease and high risk of metabolic disease are classically reported to be frequent in PsA patients (12–14,16) and our results are consistent with this finding. Nevertheless, prevalence of cardiovascular disease seems to be higher in our study and may possibly be due to the local characteristics of the population or low enrolment. In our study, 17.7% of the patients had a history of cardiovascular disease, compared to 7.6% in the study conducted by Husted *et al.* (26) on PsA patients, and 7.5% in the COMOSPA study (10) on axial and peripheral SpA patients. Moreover, 34.7% of our patients had a history of hypertension, in accordance with the current literature on PsA (15,19) and more generally on SpA (10). History of diabetes mellitus was found in 12.9% of our patients, which is comparable to previously reported data (15,19). Surprisingly, the prevalence of fibromyalgia was very low (1.6 %) and not in line with the current data in patients with PsA (32). This is

probably due to the fact that we did not use any specific tools – such as the American College of Rheumatism criteria – to collect and quantify fibromyalgia data. Indeed, in our study, data on fibromyalgia were based on both self- and physician-report.

Patients with PsA have significantly poorer health-related quality of life (QoL) than the general population (33). Using SF36 to measure QoL has been validated in PsA (34) and is common in the literature (20,26,35). Several scores are derived from the original SF36 score, such as SF12 or SF8. We chose to use the original Ware-36 (SF36) score. In our study, SF36 was given preference on account of its non-specialized nature, its assessment of the various themes of QoL, and its ease of use as part of our self-assessment questionnaire. The QoL findings in our study seem to be comparable to others found in the current literature (20,35).

Our findings show some consistency with studies that have investigated the effects of comorbidity on patient-reported health in PsA and other inflammatory rheumatic diseases. A study conducted by Husted *et al.* (26) was, to our knowledge, the first to analyze the added effect of comorbidity on QoL in PsA. In that study, the authors reported a reduction in mental function in patients with depression and anxiety. These results are consistent with our findings. Nevertheless, associations were found between patient-reported physical health and some types of comorbidities (26), contrary to our findings. In another study conducted by Kotsis *et al*, anxiety and concern about bodily symptoms attributed to the illness were independent correlates of physical QoL in PsA (18). In our study, anxiety alone accounted for 28.7% of the variance in MCS scores. MCS was also significantly associated with number of comorbidities and mRDCI score, which explained 14.0% and 4.9% of the variance in MCS respectively. As was the case in our study, Husted *et al*. (26) found that the type of comorbidity appears to have a greater impact than the number of comorbidities. In another study conducted by Rosen CF *et al.* (36), the authors found that CCI was associated with poor quality of life in both psoriasis and PsA patients (n=201 in each group).

Strengths and limitations

Important strengths of our study include its multicentric design including patients from across 3 centers from Les Hauts-de-France, and the real-life setting that enabled us to study associations between comorbid conditions and QoL. Clinical evaluations and systematic proof-reading of all medical records were performed by a single investigator (BW), which ensured that no data was missing and permitted a meaningful comparison of measures of disease activity such as PASI and DAS28-CRP. We acknowledge several limitations to our

study, including its cross-sectional nature, which only allows for the study of associations between independent variables and outcomes of interest, precluding causal inferences. In addition, the comorbidity data, especially those based on patient self-report, may represent a source of inaccuracies, even though all electronic medical files were systematically checked by the investigator to complete and rectify the self-reported data. One criticism of the mRDCI is that it does not include all possible comorbidities, although the major pulmonary and cardiovascular diseases, and depression, are captured. Moreover, we used the Disease Activity Score (DAS28-CRP) to measure the disease activity in patients with PsA. However, the DAS28-CRP is not a tool that is used specifically for this disease. Minimal Disease Activity (MDA) and DAPSA (Disease Activity Index for Psoriatic Arthritis) should be used for further studies examining the relationship between quality of life and comorbidities in patients with PsA. Another criticism is that we did not use any specific tools to collect and quantify anxiety and fibromyalgia data.

Conclusions

Increasing awareness of the impact of comorbidities in PsA and other inflammatory rheumatic diseases, and the recognition that they are suboptimally screened for and managed clinically, have resulted in several recommendations and suggest that they should be considered as part of the screening, prevention, and monitoring of these diseases. In this study, anxiety in PsA is independently associated with mental QoL, and the type of comorbidity appears to have a greater impact than the number. The impact of psychological distress on quality of life needs further attention and is of importance, since anxiety is frequently seen in PsA and may be treatable. As such, screening for anxiety, rating its severity, and managing anxiety symptoms could lead to better quality of life in patients with PsA.

List of Abbreviations:

BDMARDs: Biologic disease modifying anti-rheumatic drugs

COPD: Chronic obstructive pulmonary disease

DAS28-CRP: Disease activity score determined according to C-reactive protein and 28 joints established

FM: Fibromyalgia

IBD: Inflammatory bowel disease

MCS: Mental health component scale of SF-36

MDA: Minimal disease activity

MRDCI: Modified Rheumatic Disease Comorbidity Index

NSAID: Nonsteroidal anti-inflammatory drug

PASI: Psoriasis area severity index

PCS: Physical health component scale of SF-36

PsA: Psoriatic arthritis

QoL: Quality of life

SF36: Medical Outcomes Study Short Form-36

SpA: Spondyloarthritis

TABLES

Table 1: Patients' sociodemographic and disease characteristics

Table 2: Physical and Mental Component Summary (PCS and MCS) Scores in SF-36 questionnaire

Table 3: Relationships between confounding factors (sociodemographic variables and disease activity) and patient-reported physical and mental quality of life

Table 4: Results for univariate linear regression analysis of physical and mental health on type of comorbid condition adjusted for relevant confounders

Table 5: Results for multivariate linear regression analysis of mental health on type of comorbid condition adjusted for relevant confounders

Table 6: Results for univariate linear regression analysis of physical and mental health on number of comorbid conditions adjusted for relevant confounders

FIGURES

Supplementary Figure 1: Prevalence of the nine main comorbidities

Supplementary Figure 2: Prevalence of all comorbidities

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Table 1: Patients' sociodemographic and disease characteristics

	Mean ± SD, median or no. (%)
Age, years	52.6 ± 12.6, 54
Male sex	77 (62.1)
Body Mass Index, kg/m²	27.9 ± 5.6, 27.3
Positive HLA–B27 (n = 54)	20 (37.0)
Disease duration, years	11.3 ± 9.6, 10
In employment	55 (44.4)
Married	70 (56.4)
Education	
-Primary or lower	22 (17.8)
-Secondary	68 (54.8)
-University	34 (27.4)
Smoking status	
-Current	31 (25.0)
-Past	39 (31.5)
-Never	54 (43.5)
Presence of extra-articular manifestations	
-Uveitis	7 (5.7)
-IBD	9 (7.2)
DAS-28 CRP	2.7 ± 1.1, 2.5
DAS-28 CRP ≤ 2.6	68 (54.8)
Psoriasis Area Severity Index (PASI)	2.9 ± 5.4, 0.95
Severe psoriasis (PASI ≥ 10)	10 (8.1)
No skin involvement (PASI=0)	46 (37.1)
Treatment	
-Current biologic DMARD	88 (71.0)
-Current synthetic DMARD	43 (34.7)
-Current corticosteroid	16 (12.9)
-Current NSAID	20 (16.1)
Comorbidities	
-Excess weight (Overweight/Obesity)	87 (70.2)
-Anxiety	55 (44.4)
-Depression	36 (29.0)
-Cardiovascular disease	22 (17.7)
-Diabetes mellitus	16 (12.9)
-Osteoporosis	14 (11.3)
-COPD/Asthma	12 (9.7)
-Cancer (any)	9 (7.3)
-Fibromyalgia	2 (1.6)
Number of comorbidities (0-9)	2.0 ± 1.3, 2
≥3 comorbidities	38 (30.6)
mRDCI (0-12)	2.0 ± 1.8, 2
Charlson Comorbidity Index (CCI) (1-42)	2.4 ± 1.6, 2

SD: Standard deviation; IBD: Inflammatory bowel disease; DAS-28 CRP: Disease activity score determined according to C-reactive protein and 28 joints established; DMARD: Disease modifying anti-rheumatic drug; NSAID: Nonsteroidal anti-inflammatory drug; COPD: Chronic obstructive pulmonary disease; mRDCI: Modified rheumatic disease comorbidity index

Table 2: Physical and Mental Component Summary (PCS and MCS) Scores in SF-36 questionnaire

	Total population, n=124 Mean ± SD, Median
Physical Component Score, PCS	**41.2 ± 9.7, 40.8**
Physical function (PF)	62.3 ± 26.3, 70.0
Role limitations due to physical health problems (RP)	48.4 ± 40.9, 50.0
Bodily pain (BP)	48.9 ± 26.2, 51.0
General health perception (GH)	47.2 ± 20.2, 46.0
Mental Component Score, MCS	**43.2 ± 12.4, 47.0**
Vitality (VIT)	43.6 ± 20.6, 45.0
Social function (SF)	70.1 ± 27.5, 75.0
Role limitations due to emotional problems (RE)	59.4 ± 43.7, 66.7
General mental health (MH)	58.7 ± 21.3, 60.0

SD: Standard deviation

Table 3: Relationships between confounding factors (sociodemographic variables and disease activity) and patient-reported (a) physical and (b) mental quality of life

PCS	Mean ± SD, median or correlation coefficient (r)	P-value
Sex		0.045 *
Female	38.9 ± 10.5, 38.5	
Male	42.5 ± 9.0, 41.4	
Age (years)		0.29 **
	-0.095	
Marital status (married versus others)		0.30 *
Married	42.0 ± 9.9, 42.6	
Others	40.2 ± 9.4, 38.9	
Disease duration from the time of diagnosis (years)		0.062 ***
	0.168	
Educational status		0.11 *
University education	43.4 ± 10.6, 43.5	
Primary and secondary education	40.3 ± 9.2, 40.2	
Socio-professional category		<0.0001 *
In active employment	45.1 ± 8.5, 44.8	
Others	38.1 ± 9.5, 37.9	
DAS28-CRP		<0.0001 ***
	-0.491	
PASI		0.34 ***
	0.085	

PCS: Physical health component scale of SF-36; SD: Standard deviation; DAS-28 CRP: Disease activity score determined according to C-reactive protein and 28 joints established; PASI: Psoriasis area severity index

* Student test; ** Pearson correlation test; *** Spearman correlation test

MCS	Mean ± SD, median or correlation coefficient (r)	P-value
Sex		0.95 *
Female	43.2 ± 12.7, 45.4	
Male	43.2 ± 12.3, 47.4	
Age (years)		0.110 **
	0.144	
Marital status (married versus others)		0.57 *
Married	43.8 ± 12.5, 47.8	
Others	42.5 ± 12.4, 42.7	
Disease duration from the time of diagnosis (years)		0.075 **
	0.160	
Educational status		0.109 *
University education	46.1 ± 11.9, 48.7	
Primary and secondary education	42.1 ± 12.5, 41.9	
Socio-professional category		0.23 *
In active employment	44.9 ± 11.9, 47.9	
Others	41.9 ± 12.7, 41.1	
DAS28-CRP		0.009 **

	-0.234	
PASI		0.80 **
	-0.023	

MCS: Mental health component scale of SF-36; SD: Standard deviation; DAS-28 CRP: Disease activity score determined according to C-reactive protein and 28 joints established; PASI: Psoriasis area severity index

* Wilcoxon unpaired test; **Spearman correlation test

Table 4: Results for univariate linear regression analysis of physical and mental health on type of comorbid condition adjusted for relevant confounders

	ß (SE)	P-value	R^2
PCS			
Cardiovascular disease*	-1.31 (1.97)	0.51	0.004
Excess weight (BMI≥25kg/m²)	- 2.64 (1.56)	0.09	0.024
Diabetes mellitus	0.36 (2.19)	0.87	<0.001
Pulmonary disease (COPD/Asthma)	- 2.65 (2.46)	0.28	0.010
Osteoporosis**	- 0.68 (2.40)	0.78	0.001
Anxiety	- 0.18 (1.49)	0.90	<0.001
Depression	- 1.79 (1.72)	0.30	0.009
Malignancy	0.71 (2.82)	0.80	0.001
Fibromyalgia		NA***	
MCS			
Cardiovascular disease*	**-6.93 (2.96)**	**0.021**	**0.046**
Excess weight (BMI≥25kg/m²)	0.39 (2.43)	0.87	<0.001
Diabetes mellitus	1.03 (3.36)	0.76	<0.001
Pulmonary disease (COPD/Asthma)	**- 8.78 (3.70)**	**0.019**	**0.047**
Osteoporosis**	0.03 (3.67)	0.99	<0.001
Anxiety	**- 13.04 (1.92)**	**<0.0001**	**0.287**
Depression	**- 9.96 (2.47)**	**0.0001**	**0.124**
Malignancy	**12.53 (4.17)**	**0.003**	**0.073**
Fibromyalgia		NA***	

Confounders: Sex, age, marital status (married vs. others), disease duration from the time of diagnosis, educational status (primary and secondary education vs. university education), socio-professional category (in active employment vs. others), DAS28-CRP and PASI.

PCS: Physical health component scale of SF-36; MCS: Mental health component scale of SF-36; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; NA: Not applicable; DAS-28 CRP: Disease activity score determined according to C-reactive protein and 28 joints established; PASI: Psoriasis area severity index

* including history of ischemic disease (myocardial infarction and stroke), angina, stent, carotid atheromatous plaques and arteritis of the lower limbs
** including history of osteoporosis (defined as a T-score of less than -2.5 at any site), non-traumatic vertebral/peripheral fractures or anti-osteoporotic agent (except vitamin D and calcium)
*** Due to inadequate prevalence (1.6% of patients)

ß (SE): estimated linear coefficient with Standard Error
P-value: regression linear model adjusted with confounders
R^2: partial coefficient correlation

Table 5: Results for multivariate linear regression analysis of mental health on type of comorbid condition adjusted for relevant confounders

	ß (SE)	P-value	R^2
Cardiovascular disease*	-4.40 (2.57)	0.09	0.026
Pulmonary disease (COPD/Asthma)	-2.59 (3.22)	0.42	0.006
Anxiety	**-10.81 (2.10)**	**<0.0001**	**0.194**
Depression	-2.84 (2.45)	0.25	0.012
Malignancy	6.15 (3.69)	0.098	0.025

Confounders: Sex, age, marital status (married vs. others), disease duration from the time of diagnosis, educational status (primary and secondary education vs. university education), socio-professional category (in active employment vs. others), DAS28-CRP and PASI.

COPD: Chronic obstructive pulmonary disease; DAS-28 CRP: Disease activity score determined according to C-reactive protein and 28 joints established; PASI: Psoriasis area severity index

* including history of ischemic disease (myocardial infarction and stroke), angina, stent, carotid atheromatous plaques and arteritis of the lower limbs

ß (SE): estimated linear coefficient with Standard Error
P-value: regression linear model adjusted with confounders
R^2: partial coefficient correlation

Table 6: Results for univariate linear regression analysis of physical and mental health on number of comorbid conditions adjusted for relevant confounders

	ß (SE)	P-value	R^2
PCS			
Number of comorbidities	-1.02 (0.59)	0.089	0.025
Charlson score	-0.14 (0.56)	0.80	<0.001
mRDCI score*	-0.44 (0.43)	0.30	0.009
MCS			
Number of comorbidities	**-3.68 (0.85)**	**<0.0001**	**0.140**
Charlson score	-0.96 (0.85)	0.26	0.011
mRDCI score*	**-1.56 (0.64)**	**0.0167**	**0.049**

Confounders: Sex, age, marital status (married vs. others), disease duration from the time of diagnosis, educational status (primary and secondary education vs. university education), socio-professional category (in active employment vs. others), DAS28-CRP and PASI.

PCS: Physical health component scale of SF-36; MCS: Mental health component scale of SF-36; mRDCI: Modified rheumatic disease comorbidity index; DAS-28 CRP: Disease activity score determined according to C-reactive protein and 28 joints established; PASI: Psoriasis area severity index

* including lung diseases, cardiovascular disease (myocardial infarction, stroke or other cardiovascular disease), hypertension, ulcer or other gastrointestinal disease, diabetes mellitus, fracture, depression, malignancy, kidney disease (eGFR <60 ml/min/1.73m²), and obesity (BMI>30 kg/m² or BMI>35 kg/m²).

ß (SE): estimated linear coefficient with Standard Error
P-value: regression linear model adjusted with confounders
R^2: partial coefficient correlation