Influence of Disease Manifestations on Health-related Quality of Life in Early Psoriatic Arthritis

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ABSTRACT. ***Objective.*** Psoriatic arthritis (PsA) is a multifaceted disease. Affecting joints, skin, entheses, and dactylitis, its effect on health-related quality of life (HRQOL) could be substantial. We aim to assess HRQOL in patients newly diagnosed with PsA and analyze its associations with disease manifestations.

Methods. Data collected at time of diagnosis from patients with PsA included in the Dutch south-west Early Psoriatic Arthritis cohort (DEPAR) study were used. HRQOL was assessed using 8 domains of the Medical Outcomes Study Short Form-36 (SF-36) questionnaire. Patients were classified based on primary manifestation in arthritis subtypes (i.e., mono-, oligo-, or polyarthritis) and other subtypes (i.e., enthesitis, dactylitis, and axial disease). In all patients, presence of arthritis, enthesitis, dactylitis, psoriasis, and chronic inflammatory back pain was determined. Multivariable linear regression was used to determine associations of PsA manifestations with HRQOL.

Results. Of 405 patients, primary manifestation was peripheral arthritis in 320 (78 monoarthritis, 151 oligoarthritis, and 91 polyarthritis), enthesitis in 37, axial disease in 9, and dactylitis in 39. Mean scores of SF-36 domains were lower than the Dutch reference population and similar across arthritis subtypes. A higher number of enthesitis locations and tender joints, and presence of chronic back pain, were independently associated with worse SF-36 scores. Psoriasis and dactylitis were not associated with worse scores.

Conclusion. HRQOL was diminished in PsA at time of diagnosis compared to the Dutch reference population, and tender joints, enthesitis at clinical examination, and back pain as indicators of pain affected HRQOL. (First Release July 1 2018; J Rheumatol 2018;45:1526–31; doi:10.3899/jrheum.171406)

Key Indexing Terms:
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Psoriatic arthritis (PsA) is a spondyloarthropathy that can present with arthritis, enthesitis, psoriasis, spondylitis, and dactylitis[1]. Patients with PsA report lower health-related quality of life (HRQOL) than the general population and patients with psoriasis[2,3,4,5,6]. The reported burden of disease is substantial; however, HRQOL in PsA is studied only in patients with longstanding disease. It is unknown to what extent this burden of disease is already present at the time of diagnosis and before starting treatment. Also, very little is known about how much each disease manifestation affects HRQOL.

One of the challenges in treating PsA is the heterogeneity of manifestations. In studies analyzing the effect of clinical variables on HRQOL in patients with PsA, arthritis has been the only musculoskeletal manifestation investigated[7,8]. Among patients with PsA, arthritis was found to impair HRQOL. A study in PsA showed that psoriasis, which is known to affect HRQOL, had no additional effect on HRQOL in patients who already had PsA[8]. The Corrona registry, however, showed that patients with more skin

involvement report more pain and disability than patients with less skin involvement. In all studies evaluating the effect of PsA manifestations on HRQOL, other PsA-specific disease features such as dactylitis or enthesitis were not specifically evaluated. In making treatment decisions, it is very important to know how all PsA manifestations affect HRQOL.

The main objectives of this real-life cohort study are (1) to describe the quality of life in newly diagnosed patients with PsA, and (2) to analyze the influence of swollen and tender joints, enthesitis, dactylitis, back complaints, and skin involvement on HRQOL.

MATERIALS AND METHODS

Patients and setting. Newly diagnosed patients with PsA were invited to participate in the Dutch south-west Early Psoriatic Arthritis cohoRt (DEPAR). The diagnosis was made by rheumatologists and based on expert opinion; no classification criteria were applied, to ensure enrollment of a population representative of daily clinical practice. All eligible patients with newly diagnosed PsA [aged ≥ 18 yrs, no current treatment with disease-modifying antirheumatic drugs (DMARD) for joint complaints, and sufficient knowledge of the Dutch language] were asked to participate. Use of DMARD for psoriasis and use of nonsteroidal antiinflammatory drugs were allowed. Patients were recruited in centers in the southwest of the Netherlands (1 academic hospital, 10 general hospitals, and 1 treatment center specialized in rheumatic care). For this analysis, baseline data were used from patients included between August 2013 and November 2016. Written informed consent was obtained from all participants according to the Declaration of Helsinki. The study was approved by the local medical research ethics committee of Erasmus MC, University Medical Center Rotterdam, the Netherlands (MEC-2012-549).

Patient and disease characteristics. Trained research nurses collected clinical data, including swollen and tender joint count (66 and 68 joints, respectively), enthesitis at clinical examination [Leeds Enthesitis Index (LEI)[9] and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)[10]], dactylitis [Leeds Dactylitis Index (LDI)[11]], psoriasis [Psoriasis Area and Severity Index (PASI)[12]], and a standardized history of complaints (including duration, musculoskeletal complaints, and back complaints). Psoriasis severity was categorized as absent (PASI = 0), mild (PASI > 0 and ≤ 7), and moderate to severe (PASI > 7)[13]. Patients were classified as having chronic back pain (CBP) if they reported chronic complaints of back pain for a duration of longer than 3 months at present or in the past 12 months and with onset < 45 years of age. In these patients, fulfillment of Assessment of SpondyloArthritis international Society (ASAS) classification criteria for inflammatory back pain (IBP) was determined[14]. Disease subtype at time of diagnosis was determined by the rheumatologist and defined by primary presentation as monoarthritis (1 joint), oligoarthritis (2–4 joints), and polyarthritis (≥ 5 joints), and in case of absence of peripheral arthritis, defined as enthesitis, dactylitis, or with axial involvement. A diagnosis of enthesitis was made based on patient-reported complaints of enthesitis and entheseal pain at subsequent clinical assessment by the physician. The subtyping was based on the most prominent musculoskeletal feature at presentation as assessed by the rheumatologist. Fulfillment of ClASsification criteria for Psoriatic ARthritis (CASPAR) was determined[15].

Primary outcome of interest — HRQOL. HRQOL was assessed using the Medical Outcomes Study Short Form-36 (SF-36). This generic measure covers 8 domains: physical functioning (PF), physical role functioning (PR), bodily pain (BP), general health (GH), vitality (VI), social functioning (SF), emotional role functioning (ER), and mental health (MH). With these separate domains, the physical component summary (PCS) and mental component summary (MCS) were calculated to provide a global score[16]. The domains have a range of 0 to 100 with a higher score representing a better state and were compared to domain scores of the Dutch reference population[17]. This reference population (n = 1742) had a mean age of 47.6 years and 56% were male. The component summary scores were adjusted by the general Dutch population, resulting in norm-based scores with mean 50 (SD 10). Patients filled out their questionnaires either online (92%) or on paper, shortly before or after their visit to the research nurse.

Statistical analysis. Patient characteristics were described using simple descriptive analysis techniques. To evaluate the effect of each disease manifestation, domain scores in subgroups of arthritis (monoarthritis, oligoarthritis, and polyarthritis), enthesitis (present and absent), psoriasis (absent, mild, moderate-severe), dactylitis (present and absent), and back pain (no CBP, CBP– IBP+, and CBP– IBP–) were compared and differences were tested with Wilcoxon rank tests in case of 2 subgroups and Kruskal-Wallis tests in case of more subgroups. In subsequent univariable and multivariable linear regression analyses, we tested whether these associations were also present when adjusting the scores for the other disease manifestations. The dependent variables were the SF-36 PCS and SF-36 MCS. The SF-36 MCS was square-transformed to improve model fitting. Independent variables included in both models were age, sex, swollen joint count (66), tender joint count (68), number of enthesitis at clinical examination (LEI + MASES), presence of dactylitis (LDI > 0), PASI, and presence of IBP. Interaction terms of enthesitis at clinical examination, tender joint count, and CBP were tested. Complete cases were used in these analyses and with a sensitivity analysis, the effects of patients with missing variables were tested. The variance inflation factor was calculated in each model to test for multicollinearity. STATA 14.0 was used.

RESULTS

In November 2016, 405 patients with newly diagnosed PsA had been included. Table 1 shows patient characteristics at baseline. Mean age was 50 years (SD 13.8) and 49% were male. Median self-reported duration of complaints at time of diagnosis was 11.6 months [interquartile range (IQR) 3.9–32 mos]. The primary manifestation at time of diagnosis was monoarthritis in 78 patients (19%), oligoarthritis in 151 (37%), and polyarthritis in 91 (22%). Primary manifestation was in 37 (9%) enthesitis, 9 (2%) axial disease, and 39 (10%) dactylitis among patients without peripheral arthritis. Most patients had more than 1 feature present. In 186 of 404 patients (46%), enthesitis at clinical examination was present according to the LEI and/or MASES (40% LEI > 0 and 34% MASES > 0). Dactylitis was present in 51 patients (13%), 344 patients had active psoriasis (85%, median PASI score 2.6, IQR 1–4.7) and 57 (15%) fulfilled ASAS IBP criteria. The CASPAR criteria were fulfilled by 328 patients (81%). Of the 77 who did not fulfill CASPAR criteria, 31 (8%) had a missing rheumatoid factor (RF) status, 24 (6%) had only a history or family history of psoriasis combined with negative RF, and 9 patients had a moderately positive RF and were negative for anticyclic citrullinated protein antibody.

The 62 patients (16%) with missing baseline questionnaires were not significantly different from the other patients (Supplementary Table 1, available with the online version of this article). Overall, HRQOL was lower in patients with early PsA than in the Dutch reference population. The differences were greater in the physical domains (i.e., PF, PR, BP, and GH), while psychosocial domains (i.e., VI, SF, ER, and MH) were close to the healthy population (Figure 1A). SF-36

Table 1. Patient characteristics of DEPAR cohort (n = 405).

Characteristics	Values
Demographic characteristics	
Age, mean (SD)	50.1 (13.8)
Male, n (%)	200 (49)
Duration of complaints, months, median (IQR)	11.6 (3.9–32)
Paid employment, n (%)	216 (63)
CASPAR criteria, n (%)	328 (81)[$]
Clinical characteristics	
BMI, mean (SD)	28.1 (5.2)
Tender joint count (68), median (IQR)	3 (1–7)
Swollen joint count (66), median (IQR)	2 (1–4)
Disease subtype, n (%)	
Monoarthritis	78 (19)
Oligoarthritis	151 (37)
Polyarthritis	91 (22)
Enthesitis	37 (9)
Axial Disease	9 (2)
Dactylitis	39 (10)
Enthesitis at clinical examination	
LEI > 0, n (%)	162 (40)
LEI in case of enthesitis, median (IQR)	2 (1–3)
MASES > 0, n (%)	136 (34)
MASES in case of enthesitis, median (IQR)	2 (1–3)
Dactylitis present, n (%)	51 (13)
Psoriasis	
PASI > 0, n (%)	344 (85)
PASI in case of psoriasis, median (IQR)	2.6 (1–4.7)
Family history of psoriasis in case of no active psoriasis, n (%)	36 (60)
CBP onset < 45 yrs of age*	147 (39)
Fulfillment of IBP criteria in CBP*	57 (15)

* Data on CBP in 380 patients. [$] Rheumatoid factor status missing in 31 (8%), and 24 (6%) had only history or family history of psoriasis with negative rheumatoid factor. DEPAR: Dutch south-west Early Psoriatic Arthritis cohort; IQR: interquartile range; CASPAR: classification criteria for psoriatic arthritis; BMI: body mass index; LEI: Leeds Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Index; PASI: Psoriasis Area and Severity Index; CBP: chronic back pain, defined as presence of back pain complaints for more than 3 months at present or in the past 12 months; IBP: inflammatory back pain (criteria: ASAS criteria for IBP); ASAS: Assessment of SpondyloArthritis international Society.

scores did not differ significantly among patients with monoarthritis, oligoarthritis, or polyarthritis (Figure 1B, and Supplementary Table 2, available with the online version of this article). Patients with enthesitis at clinical examination had significantly lower scores on all SF-36 domains than patients without enthesitis at clinical examination (Figure 1C, and Supplementary Table 3). Severity of psoriasis and presence of dactylitis did not significantly influence SF-36 scores (Figure 1D and Figure 1E, and Supplementary Tables 4 and 5). Patients reporting CBP with onset before 45 years of age had significantly worse HRQOL in all domains of the SF-36 than those without. There was no significant difference in HRQOL between patients with CBP fulfilling ASAS IBP criteria and those not fulfilling ASAS IBP criteria, except for the MH domain, which is worse in patients fulfilling ASAS IBP criteria (Figure 1F; and Supplementary Table 6). Patients with enthesitis at clinical examination also reported IBP more often.

To test the independent association between disease manifestations and HRQOL, univariable and multivariable linear regression analyses of the PCS and MCS were conducted (Table 2 and Table 3). In the univariable analysis, female sex, more tender joints, more enthesitis at clinical examination, and CBP were associated with worse PCS and MCS scores. These factors remained significant in the multivariable analysis of the PCS. In the analysis of the MCS, the interaction term of enthesitis and CBP was not significant and was removed from the final model. In the final multivariable model of the MCS, female sex and tender joint count were independently associated with worse MCS scores. In the sensitivity analysis of missing data, no relevant changes of β and p values occurred.

DISCUSSION

The main objective of our study was to describe HRQOL in PsA at time of diagnosis. Compared to the Dutch reference population, HRQOL was lower in patients with PsA and especially lower in the physical domains of the SF-36. Lower levels of HRQOL were observed in patients with more tender joints, more locations of enthesitis at clinical examination, and in patients with CBP. Because patients often presented with more than 1 disease manifestation, the contribution of each manifestation was evaluated in a multivariable analysis. Tender joints, enthesitis at clinical examination, and CBP were all independently associated with worse HRQOL. Psoriasis and presence of dactylitis did not result in loss of HRQOL as measured by the SF-36.

To our knowledge, no other studies have assessed HRQOL in a stage of disease this early. Husted, *et al* reported HRQOL of 631 patients who had established PsA with moderate to severe disease activity, and also showed that PsA lowers HRQOL[7]. Similar results were seen in a study of 551 veterans with PsA[18]. Many clinical trials, however, report a higher disease activity and a lower HRQOL before starting treatment than we found[19,20,21,22]. These data cannot directly be compared to our data, because the populations probably differ in terms of disease severity and selection of patients. It does, however, indicate that PsA is a severe chronic disease that already affects HRQOL at time of diagnosis, though the effect of disease in this usual-care population is not as great as in patients in which the first disease-modifying treatment did not suffice.

Within the PsA population, presence of tender joints, enthesitis at clinical examination, and CBP were associated with worse HRQOL, which shows that pain as a consequence of inflammation is an important determinant of HRQOL. Entheseal tenderness at clinical examination reflecting enthesitis is one of the sources of pain identified. It worsens HRQOL, even in patients who already have a polyarthritis.

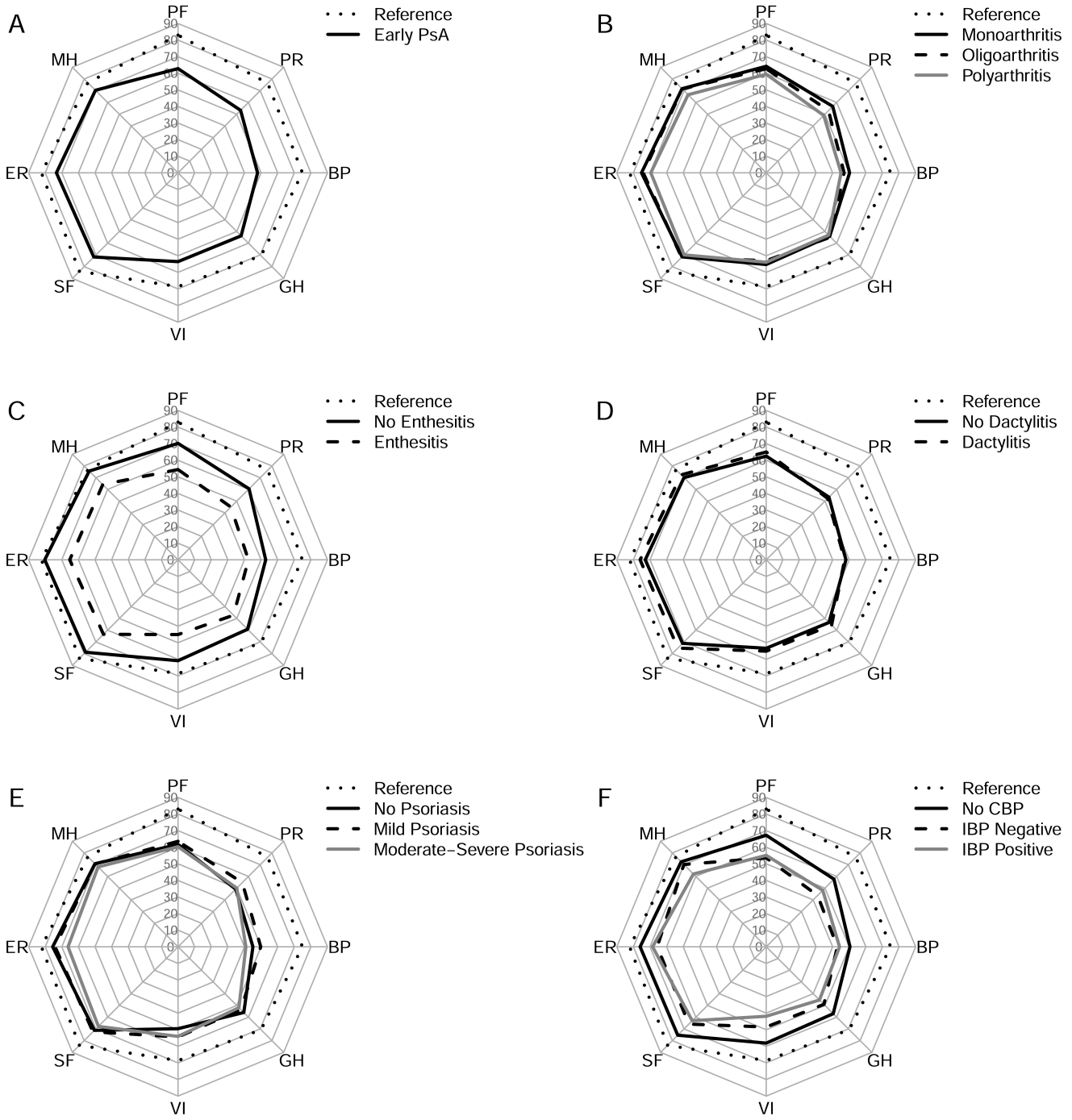

Figure 1. SF-36 domain scores in subgroups. Health-related quality of life measured by these domains of the SF-36: physical functioning (PF), physical role functioning (PR), bodily pain (BP), general health (GH), vitality (VI), social functioning (SF), emotional role functioning (ER), and mental health (MH). A. All patients. B. Arthritis subgroups. C. Enthesitis subgroups (LEI and/or MASES ≥ 0). D. Dactylitis subgroups (LDI ≥ 0). E. Psoriasis subgroups (PASI: none 0, mild 0–7, moderate/severe > 7). F. Back pain (no CBP with onset before age 45 yrs, or CBP with or without IBP). PsA: psoriatic arthritis; SF-36: Medical Outcomes Study Short Form-36; LEI: Leeds Enthesitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; LDI: Leeds Dactylitis Index; PASI: Psoriasis Area and Severity Index; CBP: chronic back pain; IBP: inflammatory back pain.

The relationship between enthesitis and HRQOL has not been investigated in PsA specifically, but some work has been done in other patients with spondyloarthritis (SpA). A study of 1505 patients with SpA, of whom 18% had PsA, showed that patients with enthesitis at clinical examination reported lower disease-specific HRQOL[23]. Other studies in axial SpA

Table 2. Univariable and multivariable linear regression analysis of SF-36 PCS.

Variables	Univariable		Multivariable	
	β	95% CI	β	95% CI
Age, yrs	–0.06	–0.13 to 0.01	–0.05	–0.12 to 0.01
Sex (male vs female)	**–3.69**	**–5.51 to –1.86**	**–2.39**	**–4.24 to –0.55**
Swollen joint count (66)	**–0.28**	**–0.55 to –0.01**	–0.07	–0.37 to 0.23
Tender joint count (68)	**–0.43**	**–0.59 to –0.26**	**–0.25**	**–0.44 to –0.05**
No. enthesitis locations	**–1.11**	**–1.47 to –0.74**	**–0.84**	**–1.25 to –0.43**
Dactylitis (no vs yes)	–0.37	–3.22 to 2.49	–0.97	–3.63 to 1.69
PASI	–0.13	–0.39 to 0.12	–0.12	–0.36 to 0.11
Chronic back pain (no vs yes)	**–2.71**	**–5.31 to –0.11**	**–5.33**	**–9.56 to –1.1**
Enthesitis × chronic back pain	–2.45	–5.48 to 0.58	**5.43**	**0.38–10.48**

Analysis of complete cases (n = 311), significant coefficients in bold face. SF-36 PCS: Medical Outcomes Study Short Form-36 physical component summary; PASI: Psoriasis Area and Severity Index.

Table 3. Univariable and multivariable linear regression analysis of SF-36 MCS (square transformation).

Variables	Univariable		Multivariable	
	β	95% CI	β	95% CI
Age, yrs	1.97	–5.50 to 9.44	1.3	–6.03 to 8.63
Sex (male vs female)	**–432**	**–632 to –231**	**–292**	**–499 to –85**
Swollen joint count (66)	5	–25 to 35	27	–6 to 61
Tender joint count (68)	**–40**	**–59 to –22**	**–38**	**–59 to –16**
No. enthesitis locations	**–93**	**–134 to –52**	–38	–83 to 7
Dactylitis (no vs yes)	118	–197 to 433	104	–195 to 402
PASI	–15	–43 to 13	–16	–43 to 10
Chronic back pain (no vs yes)	**–660**	**–987 to –333**	**–298**	**–580 to –16**

Analysis of complete cases (n = 317); significant coefficients in bold face. MCS square-transformed for a better distribution. SF-36 MCS: Medical Outcomes Study Short Form-36 mental component summary; PASI: Psoriasis Area and Severity Index.

found strong correlations between the total enthesitis score and lower scores on physical subscales of the SF-36[24,25,26]. No specific analysis in PsA was done. These and our findings suggest specific attention for enthesitis is needed in the treatment for PsA.

The validity of measuring enthesitis at clinical examination could be debated. Although joints are assessed for the presence of swelling and pain to detect arthritis, enthesitis does often not present with clearly visible signs of inflammation but with pain only. However, entheseal pain does not necessarily equal enthesitis; it could be caused by other enthesiopathies such as degenerative or metabolic processes[27]. Most cases of entheseal pain in PsA do seem to have an inflammatory origin, because it is known to resolve after biological treatment[28,29]. But in a small group of patients, it may indicate a more general pain syndrome. In our study, patients generally reported enthesitis at only 1 to 3 locations, which is less likely in the case of a general pain syndrome.

Psoriasis, present in 85% of patients, was usually mild and its influence on HRQOL was not detected with the SF-36. This may suggest that psoriasis does not affect HRQOL in PsA. In studies comparing HRQOL in PsA and rheumatoid arthritis, emotional and mental health were more affected in PsA than in rheumatoid arthritis[2,30,31] and this difference was attributed to the presence of psoriasis in patients with PsA. In patients with early PsA, we did not see an effect of psoriasis on HRQOL, possibly because at the time of diagnosis pain overshadowed skin involvement in its association with HRQOL. In addition, the effect of psoriasis symptoms such as itching and skin pain might not be detected in a general health questionnaire and may require the Dermatology Life Quality Index or Skindex.

There are several strengths and limitations to our study. One strength is that our study has a large population of patients with PsA, which makes it possible to analyze the disease in different subgroups of patients. In addition, patients with a new PsA diagnosis made by the rheumatologist were all eligible to participate if they had not yet received treatment for PsA. Our incident PsA cohort therefore reflects the population as seen in usual clinical practice, not influenced by classification criteria or criteria from trials. We were able to relate the burden of disease to the general population and compare patients with different manifestations by using the SF-36. However, by using this general questionnaire we possibly missed the disease-specific effect on HRQOL. With the data available, we were not able to distinguish CBP with inflammatory origin from lower back complaints commonly occurring in the general population[32].

Nevertheless, because the presence of CBP affects functioning, it is a sign that pain warrants attention in the treatment of PsA. Last, we only performed a cross-sectional analysis of HRQOL. Further evaluation is needed of the evolution of manifestations and subsequent change in HRQOL over time.

We found that HRQOL was diminished in PsA at time of diagnosis compared with the Dutch reference population and showed that tender joints, enthesitis at clinical examination, and presence of CBP affected HRQOL. Pain is an important determinant of functioning in early disease, and it warrants attention in the treatment of PsA.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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