

Clinical and Patient-reported Outcomes in Patients with Psoriatic Arthritis (PsA) by Body Surface Area Affected by Psoriasis: Results from the Corrona PsA/Spondyloarthritis Registry

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ABSTRACT. Objective. Psoriatic arthritis (PsA) is commonly comorbid with psoriasis; the extent of skin lesions is a major contributor to psoriatic disease severity/burden. We evaluated whether extent of skin involvement with psoriasis [body surface area (BSA) > 3% vs ≤ 3%] affects overall clinical and patient-reported outcomes (PRO) in patients with PsA.

Methods. Using the Corrona PsA/Spondyloarthritis Registry, patient characteristics, disease activity, and PRO at registry enrollment were assessed for patients with PsA aged ≥ 18 years with BSA > 3% versus ≤ 3%. Regression models were used to evaluate associations of BSA level with outcome [modified minimal disease activity (MDA), Health Assessment Questionnaire (HAQ) score, patient-reported pain and fatigue, and the Work Productivity and Activity Impairment questionnaire score]. Adjustments were made for age, sex, race, body mass index, disease duration, and history of biologics, disease-modifying antirheumatic drug, and prednisone use.

Results. This analysis included 1240 patients with PsA with known BSA level (n = 451, BSA > 3%; n = 789, BSA ≤ 3%). After adjusting for potential confounding variables, patients with BSA > 3% versus ≤ 3% had greater patient-reported pain and fatigue and higher HAQ scores (p = 2.33 × 10⁻⁸, p = 0.002, and p = 1.21 × 10⁻⁷, respectively), were 1.7× more likely not to be in modified MDA (95% CI 1.21–2.41, p = 0.002), and were 2.1× more likely to have overall work impairment (1.37–3.21, p = 0.0001).

Conclusion. These Corrona Registry data show that substantial skin involvement (BSA > 3%) is associated with greater PsA disease burden, underscoring the importance of assessing and effectively managing psoriasis in patients with PsA because this may be a contributing factor in PsA severity. (J Rheumatol First Release June 15 2017; doi:10.3899/jrheum.160963)

Key Indexing Terms:

BODY SURFACE AREA
PSORIASIS

BURDEN OF ILLNESS
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OUTCOME ASSESSMENT
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Psoriatic arthritis (PsA) is an inflammatory disease that is commonly observed in patients with psoriasis. The prevalence of PsA in the general population is 0.3%–1.0%, and its prevalence in patients with psoriasis is estimated at 10%–37%^{1,2,3}. Although arthritis may occur prior to skin disease in ~6%–18% of cases, most patients with PsA present

with skin symptoms well before arthritic symptoms^{4,5,6,7}. Some studies have shown that the extent of skin lesions is associated with the risk of PsA, and that it correlates with the severity and overall burden of psoriatic disease^{5,8,9,10}. In a recent prospective cohort study, the annual incidence for developing PsA was 2.7 cases per 100 patients with psoriasis,

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with severe psoriasis identified as the strongest independent baseline variable for subsequent PsA¹¹. Skin lesions increase the PsA burden by further reducing physical and psychosocial health-related quality of life (HRQOL)^{12,13}, raising healthcare costs¹⁴, and decreasing work productivity¹⁵.

PsA is a multidomain disease. In addition to skin lesions, it can present with dactylitis (diffuse swelling of the digits), enthesitis (inflammation at the insertion sites of tendons and ligaments), inflammatory spine disease, and other features that can affect daily functioning and HRQOL. However, there have been few studies to assess the individual contributions of these different domains.

The body surface area (BSA) affected by skin lesions may be used to measure the extent of psoriasis. A BSA > 3% provides a cutoff point for psoriasis of moderate or greater severity¹⁶, and is used in conjunction with lesion location for assessing the extent and severity of skin involvement. Studies characterizing and comparing patients with PsA with varying degrees of affected BSA have been limited^{17,18,19}. Assessment of the characteristics of PsA subpopulations defined by the extent of BSA involvement should help to expand knowledge of disease burden in these subgroups compared with the overall PsA population. The present analysis characterizes patients with PsA by the extent of their BSA affected by psoriasis (> 3% vs ≤ 3%), and evaluates the associations of affected BSA with clinical outcomes and patient-reported outcomes (PRO) in a large national observational cohort.

MATERIALS AND METHODS

Study design. This retrospective cross-sectional analysis included all patients with PsA aged ≥ 18 years who had data on BSA affected by psoriasis and were enrolled in the Corrona PsA/Spondyloarthritis (SpA) Registry during the period from March 1, 2013, to June 1, 2015. The Corrona Registry is an independent, prospective, observational cohort of patients with PsA or SpA, in which patients are recruited from more than 30 private and academic practice sites across 25 states in the United States by over 50 participating rheumatologists. As of July 2015, data on ~2300 patients with PsA and/or SpA (1567 with a diagnosis of PsA) have been collected, including information from 4700 patient visits. The total followup observation time was ~1568 patient-years, with a mean (median) patient followup of 0.7 (0.6) years.

Institutional review board approval. The Corrona Registry was approved by local institutional review boards at participating academic sites and a central institutional review board (IntegReview) for private practice sites. All patients provided written informed consent. All data were deidentified to protect patient confidentiality. Because of the design of this study, additional ethics approval was not required from the 28 participating sites.

Patient characteristics and outcomes. Data for the Corrona Registry are collected using provider and patient questionnaires at regular rheumatology office visits. Data used in our present analysis were collected at the enrollment visit. Demographic data included age, sex, and body mass index (BMI). Disease characteristics consisted of disease duration, history of comorbidities [e.g., cardiovascular disease (CVD), diabetes mellitus, any cancer, serious infections; derived from physician-reported history of comorbid conditions at enrollment], and disease activity measures, including swollen joint count in 66 joints (SJC), tender joint count in 68 joints (TJC), 28-joint Disease Activity Score with C-reactive protein (DAS28-CRP), Clinical Disease Activity Index (CDAI) score, and minimal disease activity (MDA) status. According to the Group for Research and Assessment of

Psoriasis and Psoriatic Arthritis (GRAPPA), MDA is defined as satisfying 5 of the following 7 criteria: TJC (0–68) ≤ 1, SJC (0–66) ≤ 1, BSA ≤ 3%, patient pain visual analog scale (VAS) ≤ 15, patient’s global activity VAS ≤ 20, Health Assessment Questionnaire (HAQ) score ≤ 0.5, and tender enthesal points ≤ 1²⁰. BSA assessments were performed by rheumatologists who had received previous training. For our study, a conservative definition was used for the comparison between patients with BSA > 3% vs ≤ 3%, where being in MDA was defined as satisfying 5 of the 6 criteria mentioned in the GRAPPA definition, with removal of the criterion for BSA. Hence, “modified MDA” was considered to be achieved when 5 of the remaining 6 criteria were met. PRO included HAQ scored on a 0–3 scale²¹, pain and fatigue measured on a VAS from 0 to 100 (with higher numbers indicating worse outcomes), and work productivity based on the 4 domains of the Work Productivity and Activity Impairment questionnaire (WPAI): percentage work time missed, percentage impairment while working, percentage overall work impairment, and percentage activity impairment²². Data were also collected for prior and current medication use, including use of biologics, conventional synthetic disease-modifying antirheumatic drugs (csDMARD), and prednisone.

Data analysis. Demographic characteristics, disease activity, and PRO at registry enrollment were evaluated for patients with BSA > 3% versus ≤ 3%. Between-group comparisons were made using the 2-sample Student t test for continuous variables and the chi-square test of association for categorical variables. Associations of BSA level with modified MDA status and HAQ (0–3) score were assessed with logistic and linear regression models, respectively. Patients who did not meet modified MDA requirements were placed in the adverse group. Adjusted OR and 95% CI were calculated to estimate the risk of “not being in modified MDA” for patients with PsA with BSA > 3% versus ≤ 3% at registry enrollment. Generalized linear regression models were used to assess the association of BSA status with the other PRO (pain/fatigue VAS scores and WPAI domains). Models were adjusted for the following *a priori* covariates: age, sex, race, BMI, disease duration, history of biologics use, csDMARD use, and prednisone use. In a sensitivity analysis, OR for any work or activity impairment versus no impairment (dichotomous variable) were calculated using an unadjusted model and a model adjusted with the same variables outlined above.

RESULTS

Patient demographics and baseline characteristics. Of 1567 patients with PsA enrolled in the Corrona Registry, BSA data were available for 1240 (79%) at enrollment. Of these, 451 (36%) had BSA > 3% and 789 (64%) had BSA ≤ 3%. Mean BSA involvement was 6.4% (SD 12.1%). Demographic and clinical characteristics of the overall PsA cohort and the subset with BSA data are presented in Table 1. Overall, the subset with BSA data had demographic characteristics that were comparable to the entire PsA cohort (mean age was 53.6 yrs, 50% were women, and 91% were white; data not shown). The subgroup of patients with BSA > 3% were younger (52.2 vs 54.4 yrs, $p = 0.005$) and had a greater BMI versus those with BSA ≤ 3% (32.0 mg/kg² vs 31.2 mg/kg², $p = 0.043$). Mean PsA disease durations in the BSA > 3% and ≤ 3% subgroups were 9.0 and 8.7 years, respectively. Patients with BSA > 3% were more likely to have a history of CVD, cancer, and serious infection, and significantly more likely to have a history of diabetes ($p < 0.05$). Patients with BSA > 3% also had greater PsA disease activity, as reflected by TJC (0–68; $p = 0.009$), SJC (0–66; $p < 0.0001$), DAS28-CRP ($p = 0.023$), and CDAI scores ($p < 0.0001$), and were less likely to meet modified MDA criteria ($p = 0.004$);

Table 1. Demographic and clinical characteristics and medication history of patients with psoriatic arthritis by BSA.

Characteristics	Total, N = 1567	BSA ≤ 3%, N = 789	BSA > 3%, N = 451
Demographics			
Age, yrs, mean (SD)	53.8 (13.3)	54.4 (13.2)	52.2 (13.4) [†]
Sex, n (%)			
Men	732 (48), n = 1541	372 (48), n = 777	224 (51), n = 443
Women	809 (52), n = 1541	405 (52), n = 777	219 (49), n = 443
White, n (%)	1428 (91)	722 (92)	402 (89)
BMI, mg/kg ² , mean (SD)	31.6 (7.2)	31.2 (7.0)	32.0 (7.5)*
Obese, BMI ≥ 30 kg/m ² , n (%)	788 (53), n = 1480	380 (51)	238 (55)
Disease characteristics			
Disease duration, yrs, mean (SD)	8.6 (8.9)	8.7 (8.6)	9.0 (9.4)
Dactylitis, n (%)	228 (15)	104 (13)	74 (16)
Enthesitis, n (%)	420 (27)	196 (25)	116 (25)
MDA, n (%) [‡]	417 (42), n = 989	NA	NA
Modified MDA, n (%) [‡]	NA	188 (30), n = 630	77 (21) [†] , n = 359
TJC68, median (IQR)	1 (0–5)	0 (0–4)	2 (0–7)*
SJC66, median (IQR)	0 (0–2)	0 (0–2)	1 (0–4) [§]
DAS28-CRP, mean (SD)	2.8 (1.0)	2.7 (1.0)	3.0 (1.1) [§]
CDAI, mean (SD)	11.9 (8.7)	10.7 (7.6)	13.8 (10.0) [§]
CRP, mg/l, mean (SD)	3.0 (7.2)	4.5 (10.2)	4.3 (10.2)*
HLA-B27–positive, n (%)	58 (18), n = 329	32 (19), n = 168	19 (19), n = 102
History of comorbidities, n (%)**			
Cardiovascular disease	934 (60)	469 (59)	276 (61)
Diabetes mellitus	220 (14)	97 (12)	76 (17)*
Any cancer	115 (7)	52 (7)	41 (9)
Serious infections	77 (5)	38 (5)	23 (5)
PRO measures			
HAQ, 0–3, mean (SD)	0.62 (0.65)	0.54 (0.61)	0.75 (0.7) [§]
HAQ-S, mean (SD)	0.63 (0.65)	0.56 (0.61)	0.76 (0.71) [§]
VAS pain, 0–100, mean (SD)	37.6 (29.2)	33.5 (27.8)	43.9 (30.7) [§]
VAS fatigue, 0–100, mean (SD)	40.5 (29.3)	37.8 (28.6)	44.6 (30.0) [§]
WPAI, mean (SD)			
Work time missed, %	4.2 (15.1)	2.4 (10.3)	6.0 (18.0) [†]
Impairment while working, %	16.9 (21.7)	14.1 (19.6)	22.1 (24.6) [§]
Overall work impairment, %	18.8 (23.8)	15.5 (21.2)	24.1 (26.3) [§]
Activity impairment, %	20.8 (24.3)	16.9 (21.5)	28.0 (27.6) [§]
Medication use at enrollment			
Prior biologic, n (%)	1020 (65)	517 (66)	298 (66)
No. prior biologics, mean (SD)	0.9 (0.7)	1 (0.7)	0.9 (0.7)
Prior csDMARD, n (%)	1167 (74)	604 (77)	332 (74)
Prior prednisone, n (%)	215 (14)	111 (14)	52 (12)
Current biologic use, n (%)			
None	631 (40)	317 (40)	177 (39)
Biologic monotherapy	453 (29)	223 (28)	142 (32)
Biologic + csDMARD	483 (31)	249 (32)	132 (29)
Biologic + MTX	388 (25)	200 (25)	105 (23)
Current prednisone use, n (%)	132 (8)	67 (8)	30 (7)

* $p < 0.05$, BSA > 3% vs ≤ 3%. [†] $p \leq 0.005$, BSA > 3% vs ≤ 3%. [‡] Patients with MDA met 5 of 7 criteria: TJC (0–68) ≤ 1, SJC (0–66) ≤ 1, BSA ≤ 3%, patient VAS pain ≤ 15, patient's global activity VAS ≤ 20, HAQ score ≤ 0.5, and tender enthesal points ≤ 1; for modified MDA, BSA criterion was excluded and patients met 5 of remaining 6 criteria listed above. [§] $p < 0.0001$, BSA > 3% vs ≤ 3%. ** Any cancer excludes nonmelanoma skin cancer; serious infections were defined as those leading to hospitalization or to intravenous antibiotics. BSA: body surface area; BMI: body mass index; MDA: minimal disease activity; TJC68: tender joint count in 68 joints; IQR: interquartile range; SJC66: swollen joint count in 66 joints; DAS28: 28-joint Disease Activity Score; CRP: C-reactive protein; CDAI: Clinical Disease Activity Index; PRO: patient-reported outcomes; HAQ: Health Assessment Questionnaire; HAQ-S: HAQ for the Spondylarthropathies; VAS: visual analog scale; WPAI: Work Productivity and Activity Impairment questionnaire; csDMARD: conventional synthetic disease-modifying antirheumatic drug; MTX: methotrexate; NA: not applicable; n: no. patients with available data (given in cases where this number differs from the N number in the column heading).

these patients also had a higher prevalence of dactylitis.

Most patients with PsA were receiving biologic therapy

either as monotherapy or in combination with a csDMARD, most commonly methotrexate (Table 1). Rates for current

biologic therapy and history of biologic therapy were similar between patients with BSA > and ≤ 3%. Prednisone was used by a minority of patients and at slightly higher rates among those with BSA ≤ 3%.

Associations of BSA with MDA and PRO. Compared with patients with BSA ≤ 3%, patients with BSA > 3% were more likely not to be in MDA (modified definition; OR 1.56, 95% CI 1.15–2.11, p = 0.004; Table 2). This association remained evident after adjusting for potential confounding variables (adjusted OR 1.71, 95% CI 1.21–2.41, p = 0.002; Table 2, Figure 1). In univariable analysis, mean HAQ (0–3) scores were higher in patients with BSA > 3% (0.75 vs 0.54, p = 4.02 × 10⁻⁷), indicative of a poorer functional status. Multivariable analysis revealed that patients with BSA > 3% had a mean HAQ score that was 0.20 units higher than patients with BSA ≤ 3% in the unadjusted model (95% CI 0.12–0.28, p = 4.02 × 10⁻⁷; Table 2) and 0.21 units higher in the adjusted model (95% CI 0.13–0.29, p = 1.21 × 10⁻⁷; Table 2, Figure 1), indicating that greater skin involvement was associated with significantly poorer functional status.

In the univariable analysis, patients with BSA > 3% vs ≤ 3% reported greater pain and fatigue on the VAS (mean pain score, 43.9 vs 33.5; mean fatigue score, 44.6 vs 37.8, p < 0.0001). Multivariable analysis revealed that patient-reported pain and fatigue scores were significantly higher among patients with BSA > 3%. The difference in pain scores between patients with BSA > 3% and ≤ 3% was 10.42 units

in the unadjusted model (95% CI 6.88–13.94, p = 9.24 × 10⁻⁹; Table 2) and 10.54 units in the adjusted model (95% CI 6.87–14.21, p = 2.33 × 10⁻⁸; Table 2, Figure 2). For fatigue, the difference in scores between patients with BSA > 3% versus ≤ 3% was 6.86 units in the unadjusted model (95% CI 3.44–10.29, p = 8.78 × 10⁻⁵) and 5.63 units in the adjusted model (95% CI 2.13–9.12, p = 0.002).

Univariable analysis of WPAI scores revealed that these measures were higher in patients with BSA > 3% (all p < 0.005): percentage of work time missed, percentage of impairment while working, percentage of overall work impairment, and percentage of activity impairment. On multivariable analysis, patients with BSA > 3% versus ≤ 3% also had greater mean values for percentage of work time missed, percentage of impairment while working, percentage of overall work impairment, and percentage of activity impairment in the unadjusted and adjusted models (all p < 0.05; Table 2, Figure 3A). Comparable results were seen in the sensitivity analysis when WPAI variables were evaluated as dichotomous variables in the unadjusted and adjusted models (Table 2, Figure 3B). In the adjusted models, patients with BSA > 3% versus ≤ 3% were 2.35× more likely to have missed any work time (95% CI 1.37–4.04), 2.24× more likely to have any kind of impairment while working (95% CI 1.5–3.35), 2.09× more likely to have any kind of overall work impairment (95% CI 1.37–3.21), and 1.75× more likely to have any kind of activity impairment (95% CI 1.17–2.62, all p < 0.05).

Table 2. Unadjusted and adjusted data for OR and mean differences: patients with psoriatic arthritis with psoriasis BSA > 3% vs ≤ 3%.

Variable	Unadjusted Data, BSA > 3% vs Reference of ≤ 3%	Adjusted Data*, BSA > 3% vs Reference of ≤ 3%
Association of BSA level with modified MDA status, risk of not being in modified MDA, OR (95% CI)	1.56 (1.15–2.11)**	1.71 (1.21–2.41)**
Association of BSA level with functional status measured by HAQ, β coefficient (95% CI)	0.20 (0.12–0.28)**	0.21 (0.13–0.29)**
Estimated difference in mean patient-reported VAS pain, β coefficient (95% CI)	10.42 (6.88–13.94)**	10.54 (6.87–14.21)**
Estimated difference in mean patient-reported VAS fatigue, β coefficient (95% CI)	6.86 (3.44–10.29)**	5.63 (2.13–9.12)**
WPAI: estimated differences in measures of mean work productivity, β coefficient (95% CI)		
Mean % work time missed	3.66 (1.38–5.94)**	3.25 (0.68–5.83)**
Mean % impairment while working	7.97 (4.44–11.50)**	7.23 (3.56–10.9)**
Mean % overall work impairment	8.56 (4.50–12.62)**	7.34 (3.05–11.63)**
Mean % activity impairment	11.14 (7.34–14.94)**	9.59 (5.7–13.47)**
WPAI: estimated OR of any work or activity impairment vs no impairment, %, OR (95% CI)		
Work time missed	2.49 (1.53–4.04)**	2.35 (1.37–4.04)**
Impairment while working	1.93 (1.35–2.76)**	2.24 (1.5–3.35)**
Overall work impairment	1.83 (1.26–2.70)**	2.09 (1.37–3.21)**
Activity impairment	1.74 (1.20–2.52)**	1.75 (1.17–2.62)**

* Data adjusted for age, sex, race, BMI, disease duration, history of biologic use, csDMARD use, and prednisone use. ** p < 0.05. BSA: body surface area; MDA: minimal disease activity; HAQ: Health Assessment Questionnaire; VAS: visual analog scale; WPAI: Work Productivity and Activity Impairment questionnaire.

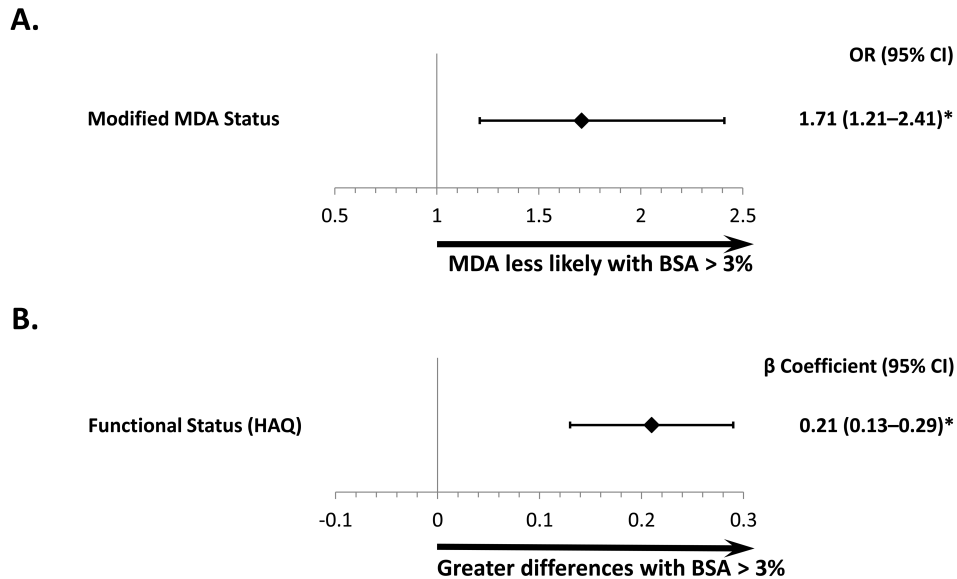


Figure 1. Association of BSA level with (A) modified MDA status (risk of not being in modified MDA) and (B) functional status measured by the HAQ. Data adjusted for age, sex, race, body mass index, disease duration, and history of biologics, conventional synthetic disease-modifying antirheumatic drugs, and prednisone use. * $p < 0.05$. BSA: body surface area; MDA: minimal disease activity; HAQ: Health Assessment Questionnaire.

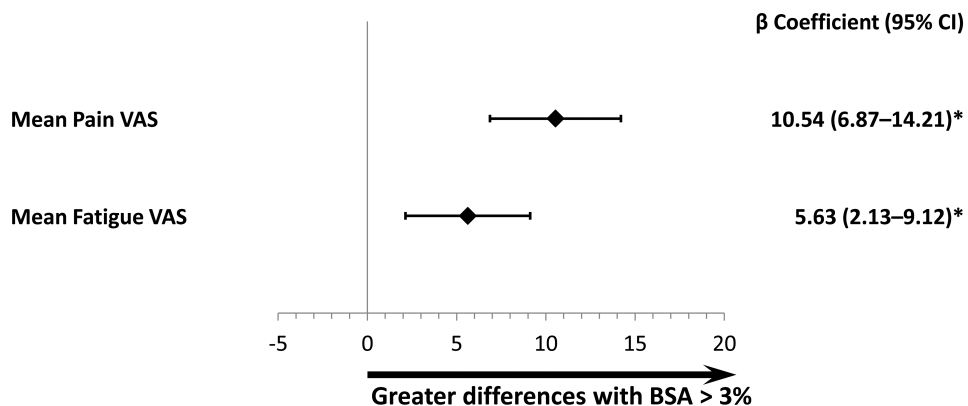


Figure 2. Adjusted model for estimated differences in mean patient-reported pain and fatigue between patients with BSA > 3% versus $\leq 3\%$. Data adjusted for age, sex, race, body mass index, disease duration, and history of biologics, conventional synthetic disease-modifying antirheumatic drugs, and prednisone use. * $p < 0.05$. BSA: body surface area; VAS: visual analog scale.

DISCUSSION

In our retrospective, cross-sectional analysis, patients with PsA with greater skin involvement (BSA > 3%) had significantly greater disease activity, lower likelihood of being in modified MDA, poorer functional status as measured by the HAQ, greater pain and fatigue, and higher overall work/activity impairment compared with their counterparts with less skin involvement (BSA $\leq 3\%$) at registry enrollment.

BSA > 3% is commonly used as a cutoff for defining psoriasis of moderate or greater severity¹⁶. In clinical studies of patients with PsA, the subset with BSA > 3% is often prospectively defined for analysis to assess treatment efficacy in those with significant psoriatic skin involvement^{23,24,25,26,27}. The results of our present study indicate that effective treatment of patients with PsA with BSA > 3% is particularly important given their greater disease burden.

In the Corrona cohort, 451 patients with PsA (36% of

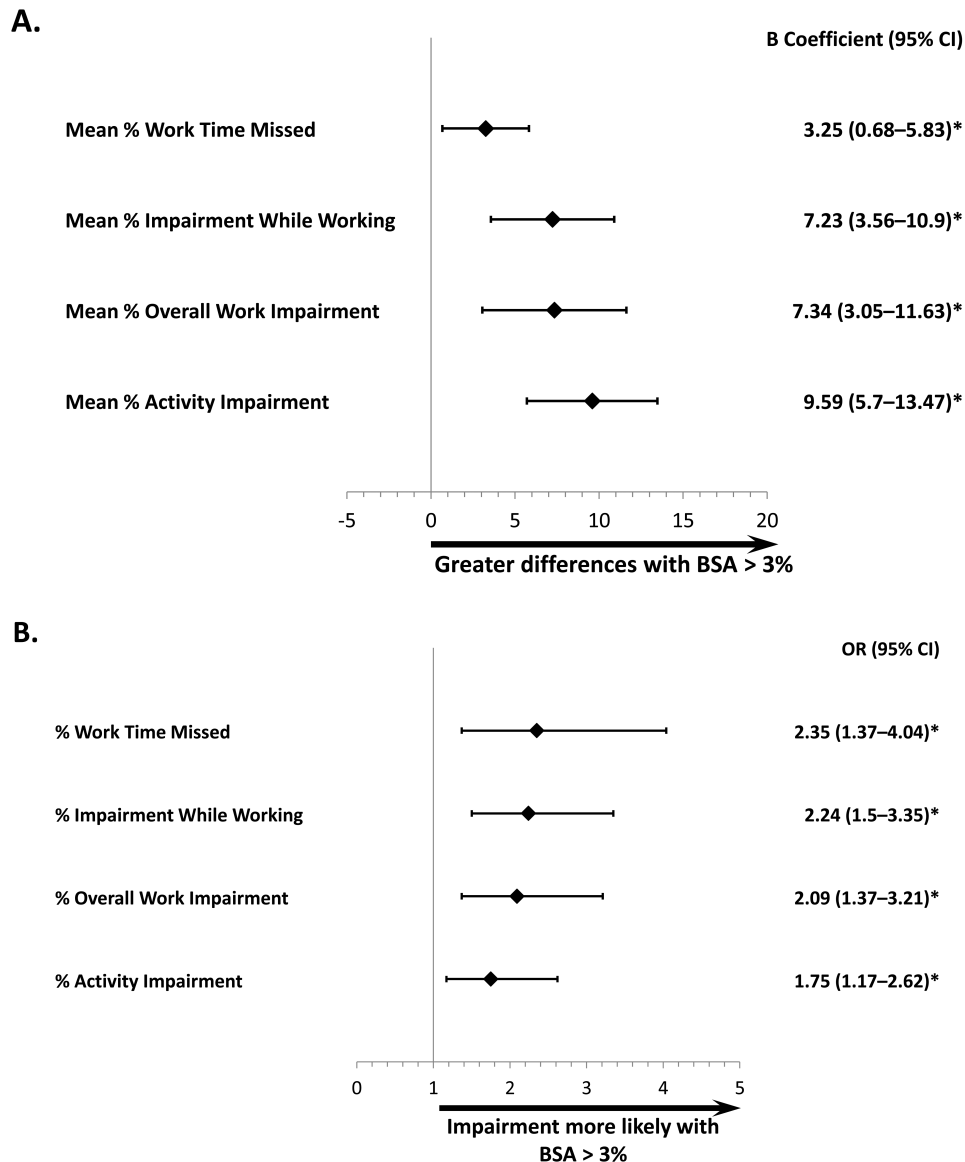


Figure 3. Adjusted model for (A) estimated differences in measures of mean work productivity and (B) estimated OR of any work or activity impairment versus no impairment between patients with BSA > 3% versus ≤ 3%. Data adjusted for age, sex, race, body mass index, disease duration, and history of biologics, conventional synthetic disease-modifying antirheumatic drugs, and prednisone use. * $p < 0.05$. BSA: body surface area.

those with BSA data or 29% of the total PsA population) had BSA affected by psoriasis > 3%. This prevalence of BSA > 3% among patients with PsA is comparable to that observed in an earlier US population-based study of 601 patients with psoriasis, of whom 71 had PsA⁵. In that study, PsA prevalence increased with greater BSA involvement, reaching 18% in patients with BSA 3%–10% and 56% in those with BSA > 10%. In clinical trial PsA populations, 50%–80% of patients typically have BSA > 3%, but they are selected based on specific eligibility criteria and therefore tend to encompass a group with greater overall psoriatic severity than those in the Corona Registry^{23,24,25,26,27}.

PRO are important in considering the burden associated with PsA because patients often rate disease activity at a higher level than clinicians²⁸. The extent of skin involvement has been correlated with the perception of psoriasis as a substantial problem by patients⁹. In our present study, patients with greater BSA involvement (> 3%) reported significantly greater pain and fatigue, had significantly poorer functional status, and had significantly greater work/activity limitations than patients with less BSA involvement. These data illustrate the higher disease burden associated with greater psoriatic skin involvement in patients with PsA. Consistent with these findings, previous studies showed that

the presence of skin lesions adds to the burden of PsA by reducing physical and psychosocial aspects of HRQOL^{12,13}.

The higher disease burden found in patients with PsA with BSA > 3% has important implications for clinical practice. It underscores the importance of placing a primary focus of PsA treatment on skin symptoms, in addition to the joint symptoms and periarticular manifestations of the disease because the extent of skin involvement may be an important factor contributing to PsA severity.

Our study is one of the first to characterize patients with PsA with skin psoriasis based on a large PsA cohort from an observational registry and to evaluate the effect of psoriasis on clinical and PRO measures in these patients in a real-world setting. However, a few limitations should be noted. First, the patients with PsA in the Corrona Registry may not be representative of the general PsA population seen in other clinical practice. Second, the study groups were identified retrospectively and therefore factors affecting outcomes may not have been fully balanced between the BSA subgroups. Although adjustments were made for a number of potential confounders, others related to disease severity could have influenced the study results. Third, patients with more severe psoriasis are likely to have more encounters with providers than those with less severe disease; thus, they have more opportunities to be diagnosed with PsA, and this may have affected the numbers of patients in the BSA subgroups (and hence, the analyses of associations between psoriasis BSA and PsA burden). Future studies should assess PsA subpopulations across the spectrum of psoriatic skin involvement (e.g., BSA ≤ 3%, BSA > 3% and < 10%, and BSA ≥ 10%) to further delineate the effect of BSA on PsA disease measures. Finally, this was a cross-sectional analysis that evaluated the effect of BSA > 3% versus ≤ 3% at the time patients were enrolled in the Corrona Registry; information regarding the extent of skin involvement and its effects on disease burden over time was not identified, so further analyses of longitudinal data may provide a more complete picture.

Even at the low BSA cutoff used in our study (> 3%), more extensive psoriatic skin involvement is associated with greater disease burden of PsA. These findings underscore the importance of assessing and effectively managing psoriasis in patients with PsA because this may be a contributing factor in PsA severity.

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REFERENCES

1. Catanoso M, Pipitone N, Salvarani C. Epidemiology of psoriatic arthritis. *Reumatismo* 2012;64:66–70.
2. Liu JT, Yeh HM, Liu SY, Chen KT. Psoriatic arthritis: epidemiology, diagnosis, and treatment. *World J Orthop* 2014;5:537–43.
3. Mease PJ, Gladman DD, Papp KA, Khraishi MM, Thaçi D, Behrens F, et al. Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. *J Am Acad Dermatol* 2013;69:729–35.
4. Armstrong AW, Schupp C, Bebo B. Psoriasis comorbidities: results from the National Psoriasis Foundation surveys 2003 to 2011. *Dermatology* 2012;225:121–6.
5. Gelfand JM, Gladman DD, Mease PJ, Smith N, Margolis DJ, Nijsten T, et al. Epidemiology of psoriatic arthritis in the population of the United States. *J Am Acad Dermatol* 2005;53:573.
6. Madland TM, Apalset EM, Johannessen AE, Rossebø B, Brun JG. Prevalence, disease manifestations, and treatment of psoriatic arthritis in Western Norway. *J Rheumatol* 2005;32:1918–22.
7. Nossent JC, Gran JT. Epidemiological and clinical characteristics of psoriatic arthritis in northern Norway. *Scand J Rheumatol* 2009;38:251–5.
8. Christophers E, Barker JN, Griffiths CE, Daudén E, Milligan G, Molta C, et al. The risk of psoriatic arthritis remains constant following initial diagnosis of psoriasis among patients seen in European dermatology clinics. *J Eur Acad Dermatol Venereol* 2010;24:548–54.
9. Lynde CW, Poulin Y, Guenther L, Jackson C. The burden of psoriasis in Canada: insights from the pSoriasis Knowledge IN Canada (SKIN) survey. *J Cutan Med Surg* 2009;13:235–52.
10. Radtke MA, Reich K, Blome C, Rustenbach S, Augustin M. Prevalence and clinical features of psoriatic arthritis and joint complaints in 2009 patients with psoriasis: results of a German national survey. *J Eur Acad Dermatol Venereol* 2009;23:683–91.
11. Eder L, Haddad A, Rosen CF, Lee KA, Chandran V, Cook R, et al. The incidence and risk factors for psoriatic arthritis in patients with psoriasis: a prospective cohort study. *Arthritis Rheumatol* 2016;68:915–23.
12. Lee S, Mendelsohn A, Sarnes E. The burden of psoriatic arthritis: a literature review from a global health systems perspective. *PT* 2010;35:680–9.
13. Rosen CF, Mussani F, Chandran V, Eder L, Thavaneswaran A, Gladman DD. Patients with psoriatic arthritis have worse quality of life than those with psoriasis alone. *Rheumatology* 2012;51:571–6.
14. Kimball AB, Guérin A, Tsaneva M, Yu AP, Wu EQ, Gupta SR, et al. Economic burden of comorbidities in patients with psoriasis is substantial. *J Eur Acad Dermatol Venereol* 2011;25:157–63.
15. Kennedy M, Papneja A, Thavaneswaran A, Chandran V, Gladman DD. Prevalence and predictors of reduced work productivity in patients with psoriatic arthritis. *Clin Exp Rheumatol* 2014; 32:342–8.
16. Van Voorhees AS, Feldman SR, Koo JY, Lebwohl MG, Menter A, Ritchlin C, et al. The psoriasis and psoriatic arthritis pocket guide - treatment algorithms and management options, 3rd ed. Portland: National Psoriasis Foundation; 2009. [Internet. Accessed May 4, 2017.] Available from: www.psoriasis.org/pocket-guide
17. Busquets-Pérez N, Rodríguez-Moreno J, Gómez-Vaquero C, Nolla-Solé JM. Relationship between psoriatic arthritis and moderate-severe psoriasis: analysis of a series of 166 psoriatic arthritis patients selected from a hospital population. *Clin Rheumatol* 2012;31:139–43.
18. Cohen MR, Reda DJ, Clegg DO. Baseline relationships between psoriasis and psoriatic arthritis: analysis of 221 patients with active psoriatic arthritis. Department of Veterans Affairs Cooperative Study Group on Seronegative Spondyloarthropathies. *J Rheumatol* 1999;26:1752–6.
19. Reich K, Krüger K, Mössner R, Augustin M. Epidemiology and clinical pattern of psoriatic arthritis in Germany: a prospective interdisciplinary epidemiological study of 1511 patients with plaque-type psoriasis. *Br J Dermatol* 2009;160:1040–7.
20. Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. *Ann Rheum Dis* 2010;69:48–53.

21. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137–45.
22. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics* 1993;4:353–65.
23. Antoni C, Krueger GG, de Vlam K, Birbara C, Beutler A, Guzzo C, et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. *Ann Rheum Dis* 2005;64:1150–7.
24. Gottlieb A, Menter A, Mendelsohn A, Shen YK, Li S, Guzzo C, et al. Ustekinumab, a human interleukin 12/23 monoclonal antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial. *Lancet* 2009;373:633–40.
25. Kavanaugh A, McInnes I, Mease P, Krueger GG, Gladman D, Gomez-Reino J, et al. Golumumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. *Arthritis Rheum* 2009;60:976–86.
26. Mease PJ, Goffe BS, Metz J, VanderStoep A, Finck B, Burge DJ. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. *Lancet* 2000;356:385–90.
27. Mease PJ, McInnes IB, Kirkham B, Kavanaugh A, Rahman P, van der Heijde D, et al; FUTURE 1 Study Group. Secukinumab inhibition of interleukin-17A in patients with psoriatic arthritis. *N Engl J Med* 2015;373:1329–39.
28. Dandorfer SW, Rech J, Manger B, Schett G, Englbrecht M. Differences in the patient’s and the physician’s perspective of disease in psoriatic arthritis. *Semin Arthritis Rheum* 2012;42:32–41.