ORIGINAL ARTICLE

Development of a New Referral Tool to Identify Psoriasis Patients with Concomitant Psoriatic Arthritis: Results of the Prospective DAPPER Cohort

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Patients with psoriasis are at risk of developing psoriatic arthritis, which can lead to joint damage. While screening questionnaires have been developed, their performance varies. The objective of this study was to develop a referral tool for dermatologists to identify psoriasis patients with concomitant psoriatic arthritis for rheumatological referral. This study used data from the DAPPER study, in which psoriasis patients were screened by a rheumatologist for the presence of concomitant psoriatic arthritis. Multivariable regression analysis was used to identify predictive variables for the presence of concomitant psoriatic arthritis: treatment history with conventional systemic drugs (odds ratio (OR) 2.97, 95% confidence interval (95% CI) 1.01–8.74, $p = 0.04$), treatment history with biologicals/small molecule inhibitors (OR 2.90, 95% CI 1.52–5.53, $p = 0.01$), patient-reported history of joint pain not caused by trauma (OR 4.23, 95% CI 1.21–14.79, $p = 0.01$), patient-reported history of swollen joints (OR 4.25, 95% CI 2.17–8.32, $p < 0.001$), and patient-reported history of sausage-like swollen digits (OR 2.38, 95% CI 1.25–4.55, $p = 0.01$). Based on these variables, a referral tool was created with an area under the curve of 0.82. This referral tool could be used to aid dermatologists to identify psoriasis patients with concomitant psoriatic arthritis, who may benefit from rheumatological referral.

Key words: psoriasis; psoriatic arthritis; screening.

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SIGNIFICANCE

Psoriasis patients are at risk of psoriatic arthritis. However, it is difficult for dermatologists to select patients who could benefit from rheumatological referral. In a dermatology psoriasis cohort, variables associated with concomitant psoriatic arthritis were identified: treatment history with: (*i*) conventional systemics, or (*ii*) biologicals/small molecule inhibitors; and patient-reported history of: (*iii*) swollen joints, (*iv*) sausage-like swollen fingers, or (*v*) joint pain not associated with trauma. Using these variables, a referral tool was developed for dermatologists to identify psoriasis patients with concomitant psoriatic arthritis. By using wide inclusion criteria and a large cohort, potential pitfalls, such as selection bias, were minimized.

One in three patients with psoriasis (PsO) attending the dermatology clinic will develop psoriatic arthritis (PsA), which can lead to disability, discomfort, and irreversible joint damage (1, 2). In the majority of patients, PsO precedes the development of PsA (3). Early treatment of arthritis is important to prevent joint damage, and to improve the physical functioning and quality of life of affected patients (4, 5). Therefore, early recognition by dermatologists and rheumatological referral of PsO patients with arthritis is crucial. Unfortunately, a considerable proportion of PsO patients with PsA are not diagnosed in clinical practice (6).

To aid dermatologists in selecting patients with a high risk of PsA, several screening questionnaires have been developed (7–15). Nevertheless, the diagnostic accuracy of these questionnaires varies widely between studies (16). For the most-studied questionnaires (Psoriatic Arthritis Screening and Evaluation (PASE) tool) (8), Psoriasis Epidemiology Screening Tool (PEST) (7), Toronto Psoriatic Arthritis Screen (ToPAS) (10)), sensitivities were in the range 24–100%, 28–92%, and 41–96%, while specificities were in the range 20–94%, 37–98%, and 30–97%, respectively (16).

Due to varying performance results, we developed a new cohort to overcome some of the problems encountered in the development of the above-mentioned tools (17). Specifically, by using an outpatient dermatology cohort with a sufficient number of PsO patients with concomitant PsA relative to the number of possible predictive parameters, we aimed to avoid overfitting (7, 14, 15) and the need to enrich the sample with PsA patients from other sources (e.g. the rheumatology department) (7, 10, 14).

The objective of this study was to develop a new referral tool to aid dermatologists in identifying PsO patients with concomitant PsA. We selected patients

with concomitant PsA in a cohort of Pso patients at the dermatology outpatient clinic. Parameters that distinguished PsO patients with and without concomitant PsA were identified and used to build a new referral tool. In addition, we explored the possibility to build a referral tool to identify PsA patients with active PsA, because these are most likely to benefit from rheumatological referral.

MATERIALS AND METHODS

Study setting and participants

We used data from the prospective observational DAPPER study, conducted at the department of dermatology of Radboud University Medical Center from June 2019 until April 2022. The study protocol and initial results have been published previously (17, 18). Briefly, 304 adult patients with PsO visiting the dermatology outpatient clinic were included. Patients were stratified 1:1:1 for current treatment modality (topicals only, conventional systemics, biologicals/small molecule inhibitors (SMI)). Patients with previously diagnosed, concomitant PsA were not excluded. Patients were screened by a rheumatologist at the dermatology outpatient clinic for signs and symptoms of PsA, using a structured interview and physical examination (Appendix S1). If PsA was suspected at study visit, and the patient was not currently treated by a rheumatologist, they were referred to a rheumatology centre for additional examinations and confirmation of PsA diagnosis. The study was approved by the medical ethics committee of the region Arnhem-Nijmegen, Radboudumc (NL68137.091.18), registered prospectively in the Dutch Trial Register (NTR 7604), and performed according to the Declaration of Helsinki and Good Clinical Practice. The current report was written according to Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) guidelines (19).

Outcome

The outcome of the prediction model was presence of concomitant PsA. A patient was classified as "PsO with concomitant PsA" if either they had been previously diagnosed by a rheumatologist, or if a (new) diagnosis of PsA was made after study referral to the rheumatology department. Patients without a previous diagnosis of PsA, and patients without signs/symptoms of concomitant PsA, or with rejection of PsA diagnosis after referral, were classified as "PsO only". Patients with "PsO with concomitant active PsA" were PsO patients with concomitant PsA who, in addition, fulfilled the following criteria at study visit: ≥ 1 swollen joint and/or active enthesitis and/or active axial spondyloarthritis. In case of suspicion of active enthesitis and/or axial spondyloarthritis, affirmation by imaging was required. Patients with "PsO with concomitant inactive PsA" were PsO patients with a previous diagnosis of concomitant PsA who did not have swollen joints, active enthesitis, or active axial spondyloarthritis at study visit.

Variables

During the study visit, the following variables were collected via structured interviews and chart reviews: demographics, intoxications, family history of PsO and PsA, treatment history, comorbidity, (previous) disease activity of skin and nails (Psoriasis Area and Severity Index (PASI), range 0–72; (20), Nail Psoriasis Severity Index (NAPSI), range 0–160 (21); Nijmegen Nail Psoriasis Activity Index Tool (N-NAIL), range 0–150 (22)); (previous) signs and symptoms of joint disease, and questions from several screening questionnaires for PsA in PsO (Early Psoriatic Arthritis Screening Questionnaire (EARP, PEST, and ToPAS)) (7, 9, 10).

Sample size

This study included patients from the DAPPER-study ($n=304$). For the prediction model, we aimed to use a maximum of 10 parameters with a restriction of 1 parameter per 10 events. Therefore, assuming a prevalence of PsA in PsO of 30% (23), the current study included 300 PsO patients.

Statistical procedures

Data were described with mean (standard deviation; SD), median (interquartile range; IQR), or absolute frequencies (percentages), where appropriate.

Possible associations between disease or patient characteristics and presence of PsA were explored using logistic regression. Missing data were not imputed. All models presented are based on complete cases.

For possible predictors, dichotomous questions (yes/no, presence/absence) were included to ease use in clinical practice. Because the study included patients with a known PsA diagnosis in the development cohort, questions referring to previous diagnosis of arthritis were not included (e.g. "Did a doctor ever tell you that you have arthritis?").

Possible predictive variables were preselected in 2 steps for entry in the multivariable model. First, univariable logistic regression was used to select variables with a $p<0.20$. Secondly, variables with overlapping concepts (based on biological plausibility and/or collinearity) were removed. Both forward and backward selection multivariable logistic regression models were employed. $p<0.05$ was considered significant in the multivariable regression models. The area under the receiver operating characteristics (ROC) curve (AUC) was used to assess the performance of the models.

Internal validity was assessed by estimating the optimism of the models using repeated K-fold cross-validation, with 10 splits and 20 repeats. A sensitivity analysis was performed, in which a scenario was created in which patients were reclassified with an uncertain diagnosis ($n=4$). These were classified as PsO with concomitant PsA in the original scenario, and in the sensitivity analysis they were classified as PsO only.

Based on the variables associated with concomitant PsA, a referral tool for dermatologists was developed. The goal of the referral tool was to alert the dermatologist when PsO patients have a high chance of concomitant PsA. If these patients are not under current rheumatological care, a referral to a rheumatologist could be considered. Test characteristics of the referral tool were tested using 2-by-2 tables to assess sensitivity and specificity.

Using the same methodology (i.e. logistic regression analysis followed by the construction of a referral tool), we explored the possibility of developing a referral tool for active PsA only. For this analysis, we compared the patient groups "PsO only" and "PsO with concomitant inactive PsA" vs "PsO with concomitant active PsA".

All analyses were performed in SPSS Statistics software version 25.0 (IBM, Armonk, NY, USA) and R studio version 3.6.2 (RStudio Inc, Boston, MA, USA) using the caret package.

RESULTS

Participants

A total of 303 PsO patients of the DAPPER study were included in this study (drop-out $n=1$). Mean age was 54 ± 16 years, 109/303 patients (36%) were female. Seventy-four

Table I. Characteristics of Patients with psoriasis (PsO) only and PsO with concomitant psoriatic arthritis (PsA)

	PsO only $n=225$	PsO + PsA $n=78$
Age, years, mean (SD)	53 (17)	54 (15)
Female sex, *n* (%)	80/225 (36)	29/78 (37)
Body mass index, kg/m^2, mean (SD)	28.6 (5.7)	29.1 (5.8)
Smoking ever, *n* (%)	159/225 (71)	50/78 (64)
Physically taxing job, *n* (%)	41/225 (18)	17/78 (22)
Trauma in the past year, *n* (%)	74/225 (33)	28/78 (36)
Family history, *n* (%)		
PsO	128/225 (57)	47/78 (60)
PsA[a]	34/224 (15)	14/78 (18)
Comorbidity, *n* (%)		
Major adverse cardiovascular event	24/225 (11)	9/78 (12)
Depression	25/225 (11)	11/78 (14)
Current therapy: No systemic	85/225 (38)	15/78 (19)
Conventional systemic drugs, *n* (%)		
All	88/225 (39)	26/778 (33)
Methotrexate	63/225 (28)	17/78 (22)
Acitretin	8/225 (4)	3/78 (4)
Fumaric acid	14/225 (6)	3/78 (4)
Cyclosporine	2/225 (1)	0/78 (0)
Biologicals/small molecule inhibitors, *n* (%)		
All	57/225 (25)	44/78 (56)
Tumour necrosis factor-inhibitor	28/225 (12)	19/78 (24)
Interleukin 17-inhibitor	9/225 (4)	12/225 (15)
Interleukin 23-inhibitor	1/225 (1)	1/78 (1)
Interleukin 12/Interleukin 23 p40 inh.	19/225 (8)	10/78 (13)
Phosphodiesterase 4-inhibitor	0/225 (0)	2/78 (3)
Skin disease, current, median (IQR)		
Age at start[b]	27 (16, 44)	23 (15, 32)
Disease duration[b]	21 (10, 35)	2.7 (1.7, 3.9)
Psoriasis Area and Severity Index[a]	2.8 (1.6, 4.5)	2.4 (1.1, 4.0)
Nail Psoriasis Severity Index[c]	15 (6, 26)	12 (5, 20)
Nijmegen Nail Psoriasis Activity Index[c]	4 (1, 10)	4 (1, 9)
Joint complaints, current, *n* (%)		
Joint pain	159/225 (71)	67/78 (86)
Back pain	95/225 (42)	41/78 (53)
Morning stiffness ≥ 30 min	26/225 (12)	19/78 (24)

[a]Missing in 1 patient with PsO only. [b]Missing in 9 patients with PsO only, and 4 patients with PsO + PsA. [c]Missing in 44 patients with PsO only, and 7 patients with PsO + PsA.
SD: standard deviation, IQR: interquartile range.

percent of patients (225/303) were classified as PsO only; 17% as having concomitant inactive PsA (50/303); and 9% as having active PsA (28/303). Clinical characteristics of the cohort are shown in **Table I**.

Identification of potential predictors for concomitant psoriatic arthritis in psoriasis patients

Univariable logistic regression was used to compare the clinical characteristics of patients with PsO only and patients with PsO with concomitant PsA (Appendix S1; Tables SII and SIII). Using a cut-off of $p<0.2$, 25 variables were deemed statistically relevant. By eliminating overlapping variables, 11 variables remained for input in the multivariable model.

Table II shows the results of multivariable logistic regression models using forward and backward selection. Both forward and backward selection showed independent association of presence of concomitant PsA with: treatment history with conventional systemics (odds ratio (OR) 2.97, 95% confidence interval (95% CI) 1.01–8.74, $p=0.04$), treatment history with biologicals/SMI (OR 2.90, 95% CI 1.52–5.53, $p=0.01$), patient-reported history of joint pain not caused by trauma (OR 4.23, 95% CI 1.21–14.79, $p=0.02$), patient-reported history of swollen joints (OR 4.25, 95% CI 2.17–8.32, $p<0.001$), and patient-reported history of sausage-like swollen digits (OR 2.38, 95% CI 1.25–4.55, $p=0.01$). Overall fit of this multivariable logistic regression model as determined by AUC was 0.83.

Table II. Results of multivariable logistic regression analysis, discriminating patients with psoriasis (PsO) only from patients with PsO with concomitant psoriatic arthritis (PsA)

	Univariable OR (95% CI)	Multivariable OR (95% CI)
Treatment history		
All conventional systemic	4.72 (1.82–12.28)	2.97 (1.01–8.74)
All biological/small molecule inhibitor	3.80 (2.21–6.52)	2.90 (1.52–5.53)
Skin disease ever: Erythroderma	1.68 (0.77–3.69)	
Nail disease ever: Holes/pits	2.32 (1.35–3.99)	
Joint complaints ever		
Non-trauma joint pain	9.30 (2.83–30.59)	4.23 (1.21–14.79)
Swollen joints	6.62 (3.65–12.01)	4.25 (2.17–8.32)
Swollen digits	4.53 (2.62–7.84)	2.38 (1.25–4.55)
Heel pain	1.54 (0.88–2.69)	
Joint complaints current		
Joint pain	2.53 (1.26–5.09)	
Back pain	1.52 (0.90–2.54)	
Morning stiffness	2.47 (1.28–4.77)	
Intercept		–4.89
Area under curve		0.83

Possible predictors for PsA in PsO patients were tested using multivariable logistic regression. After elimination of overlapping variables, predictors with a *p*-value ≤ 0.20 were inserted in the multivariable model. Odds ratios (ORs) (PsO only vs PsO with concomitant PsA) are depicted with 95% confidence interval (CI). Complete regression formulas are shown in Appendix S1; Table SVII.

Internal validation and sensitivity analyses

The optimism of the model was estimated using repeated K-fold validation. The AUC of the model was 0.83, and the AUC of the internal validation model was 0.82, giving an optimism of 0.01.

In the sensitivity analyses, patients who were not referred to the rheumatologist but did have a suspicion of PsA at study visit ($n=4$) were re-classified as PsO only instead of PsO with concomitant PsA. This analysis denoted the same 5 variables as independent predictors, as shown in Appendix S1; Table SIV.

Development of referral tool for psoriasis patients with concomitant psoriatic arthritis

Based on the results of the above-mentioned analyses, we developed a referral tool for dermatologists to help them identify Pso patients with concomitant PsA. The following variables were included: treatment history with conventional systemics, treatment history with biologicals/SMI, patient-reported history of joint pain not caused by trauma, patient-reported history of swollen joints, and patient-reported history of sausage-like swollen digits. Every variable was scored 1 point if present, and 0 points if absent. ROC curve of this 5-variable model showed an AUC of 0.82.

Table III. Test performance of referral tool for concomitant psoriatic arthritis in psoriasis patients at different cut-off points

	5 variable test	4 variable test
Cut-off ≥ 1	Sens: 99% Spec: 4%	Sens: 99% Spec: 4%
Cut-off ≥ 2	Sens: 97% Spec: 23%	Sens: 96% Spec: 32%
Cut-off ≥ 3	Sens: 88% Spec: 56%	Sens: 79% Spec: 69%
Cut-off ≥ 4	Sens: 67% Spec: 85%	Sens: 47% Spec: 92%
Cut-off ≥ 5	Sens: 35% Spec: 96%	
Area under curve	0.82	0.80

The questions in the 5 variable test are:
1. Have you ever used conventional systemic medication for your psoriasis? (i.e. methotrexate, acitretin, fumaric acid, cyclosporine).
2. Have you ever used biologicals or small molecule inhibitors for your psoriasis? (i.e. tumour necrosis factor-alpha-inhibitors, interleukin-17-inhibitors, interleukin-23-inhibitors, ustekinumab or apremilast).
3. Have you ever had joint pain that was not the result of injury?
4. Have you ever had a swollen joint (or joints)?
5. Have you had a finger or toe that was completely swollen and painful for no apparent reason?

In the 4 variable test, questions 1 and 2 were combined:
Have you ever used systemic medication (i.e. pills or injections) for your psoriasis?

To increase ease of use, and to anticipate the increased use of biologicals/SMI without earlier treatment of conventional systemics (as is recommended in treatment guidelines for PsA (24)), we also made a version in which we combined the variables "treatment history with conventional systemics" and "treatment history with biologicals/SMI " into a single variable "treatment history with systemic medication". The ROC curve of this 4-variable model showed an AUC of 0.80. **Table III** shows the sensitivity and specificity of both versions of the referral tool at different cut-off points.

Development of a referral tool for psoriasis patients with concomitant active psoriatic arthritis

Using the same methodology, we also explored the possibility to develop a referral tool to identify only PsO patients with concomitant *active* PsA. Appendix S1; Table SV shows the results of logistic regression analysis comparing the patient groups "PsO only" plus "PsO with concomitant inactive PsA" vs "PsO with concomitant active PsA". Backward selection multivariable logistic regression analysis showed independent associations of active PsA with: a treatment history with biologicals/SMI (OR 3.33, 95% CI 1.44–7.71, $p=0.01$) and current joint pain (OR 9.60, 95% CI 1.27–72.38, $p=0.03$). Overall fit of the backward selection model as determined by AUC was 0.73. Forward selection multivariable logistics regression analysis also showed independent associations with a patient-reported presence of prolonged morning stiffness (OR 2.34, 95% CI 0.96–5.70, $p=0.06$), in addition to a treatment history with biologicals/SMI (OR 2.92, 95% CI 1.24–6.88, $p=0.01$), and current joint pain (OR 7.80, 95% CI 1.02–59.72, $p=0.05$). Overall fit of the forward selected model, as determined by AUC, was 0.75. Translation of these variables into a referral tool is shown in Appendix S1; Table SVI.

DISCUSSION

In the DAPPER study, patients with PsO at the dermatology outpatient clinic were investigated for the presence of PsA (17). In this population, the current study identified 5 variables that were independent predictors for the presence of PsA: treatment history with conventional systemics, treatment history with biologicals/SMI, patient-reported history of swollen joints, patient-reported history of sausage-like swollen digits, and patient-reported history of joint pain not caused by trauma. Using these variables, a referral tool was developed to aid dermatologists in identifying PsO patients with concomitant PsA.

The referral tool included items about treatment history and musculoskeletal signs and symptoms, i.e. pain and swelling. Joint swelling is considered to discriminate between inflammatory and non-inflammatory joint diseases, while sausage-like swelling of the digits (dactylitis) is considered a hallmark of PsA (25). The item "history of joint pain not caused by trauma" is derived from the ToPAS questionnaire (10). While several other questionnaires include items enquiring about joint pain in general (8, 9, 26) or joint pain combined with redness and/or swelling (11, 13), a history of joint pain not caused by trauma is unique to ToPAS. Interestingly, in the current study cohort, a history of joint pain not caused by trauma was independently associated with concomitant PsA, while current joint pain was not. Presumably, the partial overlap of patients answering yes to both variables is the reason only one was selected using the backward/forward selection procedures.

The item "treatment history with systemic medication" has, to our knowledge, not been used previously to identify PsO patients with concomitant PsA. The relationship between the use of systemic medication and the risk of PsA is still unclear. Since the biologicals/SMI used for PsO are also effective for PsA, a protective effect is biologically plausible (27). However, PsO patients who use biologicals/SMI can still develop PsA (28). A higher burden of skin involvement is associated with a higher prevalence of PsA, and patients with more severe skin involvement are more likely to receive systemic medication (29). Moreover, patients with joint complaints are at a higher risk of PsA, and physicians might be more inclined to intensify treatment if joint complaints are present (protopathic bias) (30, 31).

Remarkably, prevalence of nail disease ever and heel complaints, 2 items which are present in many other screening questionnaires, did not reach significance in our multivariable model (16). Recently, Cui et al. tested 4 different questionnaires in a Japanese PsO population, and extracted key questions which were discriminative between PsO only and PsO with concomitant PsA. Previous nail disease and heel complaints were also not found to contribute significantly to the distinction between both

patient groups (32). In contrast, in 2014, Coates et al. (12) found nail disease and heel complaints to be contributory. We hypothesize that, while the prevalence of previous nail disease and heel complaints are indeed higher in PsO with concomitant PsA (as shown by the univariable models), this effect is overshadowed by the discriminative capabilities of the other items in the referral tool.

Ideally, any referral tool should have a balance between sensitivity and specificity. We believe that, based on the current data, the 4-variable-test (ever use of systemic medication, non-traumatic joint pain, swollen joints, and swollen fingers) with a cut-off of 3 or higher has the best characteristics for this goal. With a sensitivity of 79%, a specificity of 69% and a prevalence of 26%, this would mean that, out of 100 patients with PsO, half of the patients would be referred, of which again half would have PsA. However, 1 in 5 patients with PsA would be missed.

Comparison of the performance of our referral tool with previously designed screening questionnaires is difficult, because of the large variation in the reported performances in different studies and the different populations used to develop and evaluate these questionnaires (16). In the DAPPER cohort, psoriasis patients with previously diagnosed PsA were not excluded. Because of inclusion of these patients with known PsA, we were unable to include predictors directly related to the PsA diagnosis, such as a question enquiring about a previous arthritis diagnosis by a physician. Inclusion of predictors related to a previous diagnosis would bias the performance results of the tool, leading to an inaccurately high estimation of specificity and sensitivity. However, several previously developed screening questionnaires do contain a question enquiring about a previous diagnosis of arthritis (e.g. PEST, ToPAS, PASQ) (16). In the DAPPER cohort, the sensitivity/specificity of PEST and ToPAS were 71/81% and 75/78%, respectively (17). This is in the same range as the performance of our referral tool. However, due to the use of the "previous diagnosis" question, the performance of PEST and ToPAS in this cohort might be inaccurately high.

Because patients with currently active PsA are most likely to benefit from referral to, and thus co-treatment by, a rheumatologist, the current study also explored the option of a referral tool to identify patients with active PsA. However, the analysis was hampered by a low number of events ($n=28$ with active PsA), therefore the results must be interpreted with caution. Moreover, the performance of the model identifying active PsA only was low (AUC 0.75). Therefore, we conclude that the data gathered in our cohort were insufficient to develop a useful tool to identify patients with active concomitant PsA.

Limitations

Limitations of the current study are the setting in an academic psoriasis expertise centre, and the inclusion of patients with known PsA in the study cohort. However, inclusion of these patients also made it possible to only use patients from the dermatology outpatient clinic, without the need to "supplement" cases from a rheumatology clinic. Moreover, the use of an "unfiltered" PsO population at the dermatology clinic (e.g. including patients with and without medication, in contrast to the EARP questionnaire (9)) improved the generalizability of the current study results. Another strength is the study size, with enough events relative to the amount of possible predictive parameters, minimalizing the risk of overfitting. In the future, validation of the DAPPER referral tool in a second validation cohort should be performed, preferably in a multicentre setting involving both academic and non-academic centres.

Conclusion

With this prospective observational study a referral tool was developed to aid dermatologists in identifying PsO patients with concomitant PsA. The study showed that a patient-reported history of swollen joints, sausage-like swollen digits, joint pain not caused by trauma, and a treatment history with systemic medication are independent risk factors for the presence of concomitant PsA in patients with PsO. To improve the detection of PsO patients with concomitant PsA, future research could benefit from collaborations forming large, combined cohorts of screened PsO patients, such as the Hippocrates consortium (33). In addition, the use of clinical parameters only may not be sufficient to adequately distinguish PsO patients with and without concomitant PsA. The combination of clinical parameters with laboratory and genetic markers could also be further explored as a means of screening (34). In the meantime, use of screening questionnaires is considered a cost-effective approach to improve the care of PsO patients with (undiscovered) PsA (35).

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REFERENCES

1. Kane D, Stafford L, Bresnihan B, FitzGerald O. A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. Rheumatology (Oxford) 2003; 42: 1460–1468.
2. Haroon M, Gallagher P, FitzGerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. Ann Rheum Dis 2015; 74: 1045–1050.
3. Tillett W, Charlton R, Nightingale A, Snowball J, Green A, Smith C, et al. Interval between onset of psoriasis and psoriatic arthritis comparing the UK Clinical Practice Research Datalink with a hospital-based cohort. Rheumatology (Oxford) 2017; 56: 2109–2113.
4. Coates LC, Moverley AR, McParland L, Brown S, Navarro-Coy N, O'Dwyer JL, et al. Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. Lancet 2015; 386: 2489–2498.
5. Coates LC, Orbai AM, Morita A, Benichou O, Kerr L, Adams DH, et al. Achieving minimal disease activity in psoriatic arthritis predicts meaningful improvements in patients' health-related quality of life and productivity. BMC Rheumatol 2018; 2: 24.
6. Villani AP, Rouzaud M, Sevrain M, Barnetche T, Paul C, Richard MA, et al. Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: systematic review and meta-analysis. J Am Acad Dermatol 2015; 73: 242–248.
7. Ibrahim GH, Buch MH, Lawson C, Waxman R, Helliwell PS. Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and the development of a new instrument: the Psoriasis Epidemiology Screening Tool (PEST) questionnaire. Clin Exp Rheumatol 2009; 27: 469–474.
8. Husni ME, Meyer KH, Cohen DS, Mody E, Qureshi AA. The PASE questionnaire: pilot-testing a psoriatic arthritis screening and evaluation tool. J Am Acad Dermatol 2007; 57: 581–587.
9. Tinazzi I, Adami S, Zanolin EM, Caimmi C, Confente S, Girolomoni G, et al. The early psoriatic arthritis screening questionnaire: a simple and fast method for the identification of arthritis in patients with psoriasis. Rheumatology (Oxford) 2012; 51: 2058–2063.
10. Gladman DD, Schentag CT, Tom BD, Chandran V, Brockbank J, Rosen C, et al. Development and initial validation of a screening questionnaire for psoriatic arthritis: the Toronto Psoriatic Arthritis Screen (ToPAS). Ann Rheum Dis 2009; 68: 497–501.
11. Audureau E, Roux F, Lons DD, Bagot M, Cantagrel A, Dernis E, et al. Psoriatic arthritis screening by the dermatologist: development and first validation of the 'PURE-4 scale'. J Eur Acad Dermatol Venereol 2018; 32: 1950–1953.
12. Coates LC, Walsh J, Haroon M, FitzGerald O, Aslam T, Al BF, et al. Development and testing of new candidate psoriatic arthritis screening questionnaires combining optimal questions from existing tools. Arthritis Care Res (Hoboken) 2014; 66: 1410–1416.
13. Harle P, Letschert K, Wittig B, Mrowietz U. Sensitivity of the GEPARD patient questionnaire to identify psoriatic arthritis in patients with psoriasis in daily practice: the GEPARD-Life Study. Dermatology 2016; 232: 597–605.
14. Khraishi M, Mong J, Mugford G, Landells I. The electronic Psoriasis and Arthritis Screening Questionnaire (ePASQ): a sensitive and specific tool to diagnose psoriatic arthritis patients. J Cutan Med Surg 2011; 15: 143–149.
15. Salaffi F, Di Carlo M, Bugatti L, Lato V, Nicolini M, Carotti M. Development and pilot-testing of a new tool to screen psoriasis patients for the presence of psoriatic arthritis: the Simple Psoriatic Arthritis Screening (SiPAS) questionnaire. J Eur Acad Dermatol Venereol 2017; 31: e167–e169.
16. Urruticoechea-Arana A, Benavent D, Leon F, Almodovar R, Belinchon I, de la Cueva P, et al. Psoriatic arthritis screening: a systematic literature review and experts' recommendations. PLoS One 2021; 16: e0248571.
17. Van Hal TW, Mulder MLM, Wenink MH, Pasch MC, Van den Hoogen FHJ, Van den Reek J, et al. Discovery of psoriatic arthritis in psoriasis patients for early rheumatological referral (DAPPER) study: a prospective observational cohort. Acta Derm Venereol 2022; 102: 2225.
18. van Hal TW, Van den Reek JM, Groenewoud HM, Pasch MC, Van den Hoogen FH, Wenink MH, et al. Discovery of Arthritis in Psoriasis Patients for Early Rheumatological Referral (DAPPER): protocol for a longitudinal observational study. JMIR Res Protoc 2021; 10: e31647.
19. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD): the TRIPOD statement. Ann Intern Med 2015; 162: 55–63.
20. Fredriksson T, Pettersson U. Severe psoriasis – oral therapy with a new retinoid. Dermatologica 1978; 157: 238–244.
21. Rich P, Scher RK. Nail Psoriasis Severity Index: a useful tool for evaluation of nail psoriasis. J Am Acad Dermatol 2003; 49: 206–212.
22. Klaassen KM, van de Kerkhof PC, Bastiaens MT, Plusje LG, Baran RL, Pasch MC. Scoring nail psoriasis. J Am Acad Dermatol 2014; 70: 1061–1066.
23. Mease PJ, Gladman DD, Papp KA, Khraishi MM, Thaci 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: 729–735.
24. Singh JA, Guyatt G, Ogdie A, Gladman DD, Deal C, Deodhar A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheumatol 2019; 71: 5–32.
25. Kaeley GS, Eder L, Aydin SZ, Gutierrez M, Bakewell C. Dactylitis: a hallmark of psoriatic arthritis. Semin Arthritis Rheum 2018; 48: 263–273.
26. Garg N, Truong B, Ku JH, Devere TS, Ehst BD, Blauvelt A, et al. A novel, short, and simple screening questionnaire can suggest presence of psoriatic arthritis in psoriasis patients in a dermatology clinic. Clin Rheumatol 2015; 34: 1745–1751.
27. Gisondi P, Bellinato F, Targher G, Idolazzi L, Girolomoni G. Biological disease-modifying antirheumatic drugs may mitigate the risk of psoriatic arthritis in patients with chronic plaque psoriasis. Ann Rheum Dis 2022; 81: 68–73.
28. van Muijen ME, van Hal TW, Groenewoud HMM, van den Reek J, de Jong E. The skin may clear but the arthritis won't disappear: focusing on concomitant and new-onset psoriatic arthritis in a daily practice cohort of psoriasis patients on biologic therapy. Psoriasis (Auckl) 2020; 10: 29–37.
29. Ogdie A, Shin DB, Love TJ, Gelfand JM. Body surface area affected by psoriasis and the risk for psoriatic arthritis: a prospective population-based cohort study. Rheumatology (Oxford) 2022; 61: 1877–1884.
30. Eder L, Polachek A, Rosen CF, Chandran V, Cook R, Gladman DD. The development of psoriatic arthritis in patients with psoriasis is preceded by a period of nonspecific musculoskeletal symptoms: a prospective cohort study. Arthritis Rheumatol 2017; 69: 622–629.
31. Meer E, Merola JF, Fitzsimmons R, Love TJ, Wang S, Shin D, et al. Does biologic therapy impact the development of PsA among patients with psoriasis? Ann Rheum Dis 2022; 81: 80–86.

32. Cui R, Chen M, Li X, Wang Q, Tong Q, Zhang H, et al. Assessment of four screening tools and retrieval of key questions to detect undiagnosed psoriatic arthritis in Chinese patients with psoriasis: a multicenter study. J Dermatol 2022; 49: 615–623.
33. FitzGerald O, Pennington SR. HIPPOCRATES: improving diagnosis and outcomes in psoriatic arthritis. Nat Rev Rheumatol 2022; 18: 123–124.
34. Mulder MLM, van Hal TW, Wenink MH, Koenen H, van den Hoogen FHJ, de Jong E, et al. Clinical, laboratory, and genetic markers for the development or presence of psoriatic arthritis in psoriasis patients: a systematic review. Arthritis Res Ther 2021; 23: 168.
35. Iragorri N, Hazlewood G, Manns B, Bojke L, Spackman E, Early detection to improve outcome in people with undiagnosed psoriatic arthritis study G. model to determine the cost-effectiveness of screening psoriasis patients for psoriatic arthritis. Arthritis Care Res (Hoboken) 2021; 73: 266–274.
36. Sieper J, van der Heijde D, Landewe R, Brandt J, Burgos-Vagas R, Collantes-Estevez E, et al. New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). Ann Rheum Dis 2009; 68: 784–788.
37. Maksymowych WP, Mallon C, Morrow S, Shojania K, Olszynski WP, Wong RL, et al. Development and validation of the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index. Ann Rheum Dis 2009; 68: 948–953.
38. Healy PJ, Helliwell PS. Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures and development of an instrument specific to psoriatic arthritis. Arthritis Rheum 2008; 59: 686–691.