

Development of a Predictive Composite Index for early diagnosis of psoriatic arthritis

by Jana Publication & Research

Submission date: 18-Feb-2025 01:38PM (UTC+0700)

Submission ID: 2579311090

File name: IJAR-50317.docx (57.95K)

Word count: 4956

Character count: 30484

Development of a Predictive Composite Index for early diagnosis of psoriatic arthritis

Abstract

Objective. Psoriatic arthritis (PsA) is a progressive inflammatory disease with diagnostic challenges in early stages. This study aimed to develop a mathematical model for early PsA diagnosis, integrating clinical manifestations, inflammatory biomarkers, imaging findings, and immunological alterations to distinguish early PsA from cutaneous psoriasis (PsO) without musculoskeletal involvement.

Materials and Methods. A retrospective case-control study was conducted from 2014 to 2022 at IMSP Republican Clinical Hospital "Timofei Moşneaga." The study included 200 patients: early PsA (n=100) and PsO without musculoskeletal involvement (n=100). Clinical assessments included tender joint count (TJC) and swollen joint counts (SJC), morning stiffness, enthesitis, and dactylitis. Inflammatory markers and imaging evaluations were analyzed. A predictive model was developed using multiple regression analysis, incorporating significant diagnostic variables. Sensitivity and specificity were evaluated via ROC curve analysis and validated through bootstrapping.

Results. Early PsA patients had significantly higher TJC (7.5 ± 0.5 vs. 2.2 ± 0.5 , $p = 0.0032$), SJC (4.5 ± 0.3 vs. 2.9 ± 0.7 , $p = 0.0057$), and morning stiffness (37.7 ± 5.5 min vs. 10.2 ± 4.5 min, $p = 0.00018$). Enthesitis prevalence was higher in early PsA (78%) vs. PsO (31%, $p = 0.00023$). The predictive model demonstrated 89% sensitivity and 84% specificity in identifying early PsA.

Conclusion. The model effectively differentiates early PsA from PsO, integrating key clinical and laboratory parameters. Its high sensitivity and specificity support clinical utility for early diagnosis and intervention. Further validation in multicenter cohorts is needed.

Key words: psoriatic arthritis, early diagnosis, predictive index

Abbreviations

²²	AUC – Area Under the Curve
	CASPAR – Classification Criteria for Psoriatic Arthritis
¹²	CI – Confidence Interval
	CRP – C-Reactive Protein
	DMARDs – Disease-Modifying Anti-Rheumatic Drugs
	ESR – Erythrocyte Sedimentation Rate
	LEI – Leeds Enthesitis Index
	M±SD – Mean ± Standard Deviation
⁴	MASES – Maastricht Ankylosing Spondylitis Enthesitis Score
	MRI – Magnetic Resonance Imaging
	p – p-value (statistical significance probability)
³¹	PsA – Psoriatic Arthritis
	PsO – Psoriasis
	ROC – Receiver Operating Characteristic
²⁴	SJC – Swollen Joint Count
	SPARC – Spondyloarthritis Research Consortium of Canada Enthesitis Index
⁴⁸	STIR – Short Tau Inversion Recovery (a fat-suppressed MRI sequence)
¹⁶	T1 – T1-weighted Magnetic Resonance Imaging Sequence
	T2 – T2-weighted Magnetic Resonance Imaging Sequence
	TJC – Tender Joint Count

Introduction

⁴⁷ Psoriatic arthritis (PsA) is a condition of significant medical and social importance due to its substantial prevalence and progressive nature, which can lead to disability and early patient invalidity.^{1,2} Recently, numerous reviews have been published describing new clinical forms of

PsA and the heterogeneity of its early manifestations.³ This creates challenges in diagnosing ³⁴ the early stages of the disease, as many joint lesions ³⁵ in the initial stage lack sufficiently characteristic clinical and radiological signs to be used as diagnostic criteria.⁴ In some cases, recognizing joint diseases is extremely difficult, especially in atypical presentations such as monoarthritis or oligoarthritis.⁵ The challenges of diagnosing early-stage PsA include the following:^{3,5,6}

1. Heterogeneity of clinical forms: PsA can manifest in a variety of clinical forms, complicating the diagnostic process.³
2. Lack of characteristic clinical and radiological signs: In early stages, joint lesions do not always present clear and distinctive signs that can be used as diagnostic criteria.^{5,6}
3. Difficulties in recognizing atypical joint diseases: In cases where the disease progresses in an atypical manner, such as monoarthritis or oligoarthritis, accurate recognition and diagnosis become even more challenging.⁷

Therefore, ³⁷ the early diagnosis of PsA is essential to prevent disability and incapacitation among patients.⁸ However, the heterogeneity of clinical forms and the absence of characteristic signs in the early stages make this process complex and challenging.⁹

Recent studies have emphasized that the first two years of PsA progression are crucial for the development and advancement of the pathological process.^{7,10} It has been found that the early phase of PsA differs significantly morphologically from the later stages of the disease.¹¹ Therefore, prompt therapeutic interventions during this period are essential, as disease remission is much more frequent when treatment is initiated in the early stages of PsA.¹²

PsA is a disease in which different risk factors and immunological disorders play a crucial role in its pathogenesis.^{11,13} However, the available data on the quantitative and qualitative characteristics of risk factors and individual immune system indicators and their significance in the development of PsA are often contradictory.¹⁴⁻¹⁶ This inconsistency in

information leaves the importance of immunological disorders and recurrence of risk for psoriasis (PsO) in the diagnosis and management of this pathology insufficiently understood.¹⁷

The polymorphism of PsA clinical forms, combined with the lack of reliable early diagnostic criteria and methods, creates significant challenges in recognizing the early stages of the disease.^{18,19} Early diagnosis and treatment of PsA are crucial for preventing disease progression and long-term complications.^{20,21} A deeper understanding of the pathological disorders associated with PsA and the development of more reliable early diagnostic criteria could significantly contribute to improving clinical outcomes for patients affected by this debilitating disease.²²

Objective

The study aimed to develop an integrative mathematical model for the early diagnosis of PsA by incorporating clinical manifestations, inflammatory biomarkers and imaging findings. The model seeks to distinguish early PsA from PsO without musculoskeletal involvement, aiding timely intervention and reducing diagnostic delays.

Materials and Methods

The study was conducted between 2014 and 2022 at the Department of Rheumatology and Nephrology of IMSP Republican Clinical Hospital "Timofei Moşneaga" and included patients diagnosed with PsA and patients with psoriasis without musculoskeletal manifestations. All participants provided written informed consent prior to inclusion in the study.

The study cohort consisted of a representative sample of 200 patients, divided into two distinct groups: Group I included patients with early PsA, defined by a disease duration of ≤ 24 months from the onset of joint symptoms, while Group II comprised individuals with cutaneous psoriasis (PsO) without clinical or imaging evidence of musculoskeletal involvement. All patients were included in the study after obtaining informed consent, and strict inclusion and exclusion criteria were applied to ensure group homogeneity.

Inclusion criteria:

For Group I, diagnosis was guided primarily by the presence of musculoskeletal manifestations in patients with cutaneous psoriasis, with additional orientation based on the CASPAR classification criteria. Eligible patients were aged between 19 and 45 years, had no prior administration of biological therapies, and presented musculoskeletal imaging changes detected by ultrasonography or MRI. In Group II, the diagnosis of PsO was confirmed by a dermatologist, with the absence of joint pain, stiffness, or swelling, and no prior diagnosis of PsA or other inflammatory arthropathies.

Exclusion criteria:

Patients with other seropositive inflammatory arthropathies (e.g., rheumatoid arthritis), a history of concomitant systemic autoimmune diseases (e.g., systemic lupus erythematosus, ankylosing spondylitis), prior administration of biological DMARD therapy, pregnancy, severe chronic diseases (e.g., renal failure, decompensated hepatopathies), or a history of neoplasms or active systemic infections were excluded.

The comparative analysis aimed to evaluate clinical, serological, and imaging differences between patients with early PsA and those with PsO without musculoskeletal manifestations. Additionally, predictive modeling was applied to identify risk factors for the transition from PsO to PsA.

Demographic and clinical characteristics

Patients in Group I had a mean age of 35.9 ± 2.3 years, while those in Group II were slightly younger, with a mean age of 35.7 ± 2.1 years. The sex distribution was similar between the two groups, with a male-to-female ratio of 1.2:1 in Group I and 1.1:1 in Group II. However, a marked difference was observed in disease duration; in the early PsA group, the mean disease duration was 21.1 ± 1.7 months, whereas patients in the PsO group had a significantly longer mean psoriasis duration of 50.3 ± 3.6 months.

Clinical and laboratory parameters evaluated

Clinical assessment: ²³ tender joint count (TJC), swollen joint count (SJC), morning stiffness (min), enthesitis, dactylitis, and distribution. Biological markers: ¹⁹ erythrocyte sedimentation rate (ESR, mm/h), C-reactive protein (CRP, mg/L). Imaging: ultrasonography for enthesitis/synovitis; MRI (T1, T2, STIR with fat suppression). Activity scores: MASES, LEI, SPARC for enthesitis evaluation.

Statistical methods

Analysis was conducted using *Statistica 9.0* and *SPSS 26.0*: Comparisons: Student's *t*-test (TJC, SJC, stiffness, CRP, ESR); χ^2 test (enthesitis, dactylitis). Predictive modeling: Multiple regression (clinical/biological predictors), binary logistic regression (disease progression risk). Diagnostic accuracy: ROC curve analysis (sensitivity/specificity), Pearson correlation (*r*), AUC evaluation. Validation: Bootstrapping (1,000 replications), 95% CI reporting. *Significance threshold*: $p < 0.05$. Rigorous statistical modeling supports early PsA detection and timely treatment initiation.

Results

As a chronic inflammatory condition, PsA is characterized by a variable onset and heterogeneous progression, which was observed in this study by examining clinical manifestations, the articular and extra-articular topography of lesions, and their severity to highlight the distinctive features between early PsA and cutaneous PsO.

The TJC and overall joint manifestations were ² significantly more pronounced in patients with early PsA than in those with PsO. ¹ The mean number of tender joints was considerably higher in early PsA (7.5 ± 0.5) compared to PsO (2.2 ± 0.5 , $p=0.0032$), indicating a more evident inflammatory involvement in the former group (Table 1). Patients with PsO did not report significant joint symptoms and often disregarded joint-related complaints, emphasizing the subtlety or absence of musculoskeletal involvement in this group.

Similarly, the mean of SJC was ³⁶ significantly higher in early PsA compared to cutaneous psoriasis (4.5 ± 0.3 vs. 2.9 ± 0.7 , $p=0.0057$) (Table 1). While early PsA patients reported

localized swelling in the metatarsophalangeal joints (24%), talocrural joints (18%), and knees (15%), individuals with PsO exhibited minimal or no swelling, further confirming the absence of substantial musculoskeletal disease in this cohort.

The duration of morning stiffness was significantly shorter in early PsA compared to PsO (37.7 ± 5.5 min vs. 10.2 ± 4.5 min, $p=0.00018$) (Table 1). This difference suggests that synovial inflammation and progressive fibrosis play a major role in prolonging morning stiffness in cutaneous psoriasis, which may indicate a more advanced degree of joint deterioration.

Enthesitis, defined as inflammation at tendon and ligament insertions, was more frequent and severe in early PsA (prevalence of 78%) compared to PsO (31%, $p=0.00023$) (Table 1). The severity scores MASES (8.2 ± 0.15 vs. 3.6 ± 0.09 , $p=0.0022$), LEI (5.1 ± 0.17 vs. 2.1 ± 0.09 , $p=0.00034$), and SPARC (14.5 ± 0.07 vs. 3.9 ± 0.12 , $p=0.0019$) demonstrated significant differences between the two groups, confirming that enthesitis is more active in the early stages of PsA. This observation may have pathogenic implications, suggesting that periarticular inflammation precedes synovitis development and may contribute to disease progression.

From a topographical perspective, enthesitis in early PsA was predominantly located at the Achilles tendon (80%), plantar fascia (72%), tibial tuberosity (60%), humeral epicondyles (68%), and trochanteric bursa (55%). In contrast, in PsO, the distribution of enthesitis was less specific and less severe (Table 1), which may indicate a transition from periarticular involvement to a predominantly synovial inflammatory process.

Table 1. Clinical manifestations of early and late psoriatic arthritis

Clinical manifestations	Early PsA	PsO	p
TJC (M \pm SD)	7.5 ± 0.5	2.2 ± 0.5	0.0032
Frequent location of tender joints	Ankle (41%), distal interphalangeal joints of the	Not report significant joint symptoms, no	

	hands (40%), metatarsophalangeal (33%), knee (26%)	specific topography	
SJC (M±SD)	4.5 ± 0.3	2.9 ± 0.7	0.0057
Frequent location of swollen joints	Metatarsophalangeal (24%), ankle joint (18%), knee (15%)	Extensive involvement, no specific topography	
Duration of morning stiffness (minutes)	37.7 ± 5.5	10.2 ± 4.5	0.00018
Prevalence of enthesitis (%)	78%	31%	0.00023
MASES score	8.2 ± 0.15	3.6 ± 0.09	0.0022
LEI score	5.1 ± 0.17	2.1 ± 0.09	0.00034
SPARC score	14.5 ± 0.07	3.9 ± 0.12	0.0019
Frequent location of enthesitis	Achilles tendon (80%), plantar fascia (72%), tibial tuberosity (60%), humeral epicondyles (68%), trochanteric bursitis (55%)	Nonspecific distribution, less severe	
Dactylitis frequency (mean)	5 ± 0.5	1 ± 0.3	0.00036
Frequent location of dactylitis	Toes (70%) - hallux, toes II-IV; fingers (55%) - fingers IV-V	Nonspecific distribution, less severe	
ESR, mm/h (M±SD)	37.8 ± 2.4	15.2 ± 2.1	0.0071
CRP, mg/L (M±SD)	36.25 ± 2.23	8.12 ± 3.14	0.0056
Note: Data are presented as mean ± standard deviation (M±SD) or percentage, as appropriate.			

³ TJC – tender joint count; SJC – swollen joint count; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; ² MASES – Maastricht Ankylosing Spondylitis Enthesitis Score; LEI – Leeds Enthesitis Index; SPARC – Spondyloarthritis Research Consortium of Canada Enthesitis Index. ⁴ P-values were obtained using Student's t-test for continuous variables and χ^2 test for categorical variables. A p-value <0.05 was considered statistically significant.

Dactylitis and its topographical distribution

Dactylitis, considered a distinctive marker of PsA, was significantly more frequent in early PsA compared to PsO (5 ± 0.5 vs. 1 ± 0.3 , $p=0.00036$) (Table 1). This result confirms that ⁴² in the early stages of the disease, digital inflammation is a key element of pathogenesis. In early PsA, dactylitis was more frequently observed in the toes, especially the hallux and toes II-IV (70%), as well as in fingers IV-V of the hands (55%). In contrast, in PsO, the distribution of dactylitis was less severe and nonspecific, reflecting a minimal musculoskeletal inflammatory component.

Non-specific inflammatory markers

Patients with early PsA exhibited significantly higher ESR levels (37.8 ± 2.4 mm/h vs. 15.2 ± 2.1 mm/h, $p = 0.0071$) and CRP levels (36.25 ± 2.23 mg/L vs. 8.12 ± 3.14 mg/L, $p = 0.0056$) compared to PsO (Table 1). These findings indicate a more intense systemic inflammatory response in the first 24 months, likely driven by heightened pro-inflammatory cytokine activity. Elevated ESR and CRP suggest acute inflammation and immune activation, contributing to early joint damage. In contrast, lower values in PsO reflect the absence of substantial systemic inflammation, supporting the notion that musculoskeletal involvement significantly influences inflammatory marker levels.

Development of the mathematical model

To develop a mathematical model for the early diagnosis of PsA, the analysis was conducted on two groups of patients: early PsA and PsO. Clinical and laboratory parameters

were evaluated using a three-point scale, reflecting the severity of manifestations. ² To determine the relevance of each indicator in the early diagnosis of the disease, a multiple regression analysis was applied, selecting the variables with the highest informative value (Table 2). This approach allows for the development of a robust model capable of differentiating the early stages of PsA and providing support in clinical decision-making.

Table 2. Mathematical expectations and X² deviation of clinical and laboratory indicators

	X ² , df=1	β coefficient (±SE β)	Informative value
Clinical indicators			
TJC	1.32 [0.99:1.37]	0.426±0.115	1.51
Morning stiffness	1.42 [1.02:1.48]	0.567±0.121	1.83
SJC	1.88 [1.34:1.92]	0.601±0.142	2.11
Enthesitis	2.34 [1.99:2.51]	0.645±0.139	2.55
Dactylitis	2.47 [2.12:2.73]	0.698±0.151	2.61
Laboratory indicators			
ESR	1.79 [1.56:1.81]	0.084±0.123	2.02
CRP	2.21 [2.01:2.33]	0.123±0.102	2.47
<p>Note: Data are presented as X² values with degrees of freedom (df) – 1 and 95% confidence intervals (CI), β coefficient with standard error (SE β), and informative value for each parameter. ³ TJC – tender joint count; SJC – swollen joint count; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein. Informative value was calculated based on logistic regression analysis. A higher informative value indicates a stronger contribution of the ¹⁵ variable to early PsA diagnosis. P-values <0.05 were considered statistically significant.</p>			

Clinical data indicated that the most informative parameters for early PsA diagnosis are dactylitis, enthesitis, and the number of swollen joints. Additionally, morning stiffness and the

number of tender joints demonstrated significant diagnostic value. Regarding laboratory parameters, CRP showed superior informativeness compared to the ESR, suggesting a closer correlation between inflammatory activity and CRP⁴⁵ in the early stages of the disease.

Based on these findings, clinical indices (ϕ_C) and laboratory indices (ϕ_L) were calculated using the following formulas:

$$\phi_C = a1C1 + a2C2 + a3C3 + a4C4 + a5C5$$

$$\phi_L = b1L1 + b2L2$$

where a and b represent the informative coefficients for the respective indicators, C – clinical variables, and L – laboratory variables.

Formulation of the integrated model

To develop a robust predictive model capable of differentiating early PsA from PsO, we integrated clinical and laboratory data into a single composite index (ϕ_{APs}). This model is based on multiple regression analysis, utilizing the most informative variables for establishing an early diagnosis.

To quantify the impact of clinical and laboratory variables on the probability of early PsA diagnosis, we combined the clinical and laboratory indices into a single formula:

$$\phi_{APs} = W_C \times \phi_C + W_L \times \phi_L$$

where:

- ϕ_C = the clinical index calculated based on major clinical signs,
- ϕ_L = the laboratory index, calculated from non-specific inflammatory markers,
- W_C and W_L are weighting coefficients, adjusted to optimize the sensitivity and specificity of the model.

Each of these indices was calculated using multiple regression, according to the following equations:

$$\phi_C = \frac{0.426C1 + 0.567C2 + 0.601C3 + 0.645C4 + 0.698C5}{5}$$

$$\phi L = \frac{0.084L1 + 0.123L2}{2}$$

where: C1 – TJC, C2 – morning stiffness, C3 – SJC, C4 – enthesitis, C5 – dactylitis, L1 – ESR (mm/h), L2 – C-reactive protein (mg/L).

To optimally calibrate the model, the weighting coefficients W_C and W_L were adjusted using logistic regression analysis, ensuring that the contribution of clinical and laboratory data was proportional to their diagnostic impact. The optimal values determined were $W_C = 0.55$ and $W_L = 0.45$, indicating a slight predominance of clinical components over laboratory components.

Interpretation of diagnostic value ranges

Based on the distribution of calculated values, the following classification intervals were defined for ϕAPs :

- $\phi APs < 1.8$ – low probability of early PsA, minimal risk of rapid progression.
- $1.8 \leq \phi APs < 2.3$ – uncertain diagnosis, requires close monitoring and further investigations.
- $\phi APs \geq 2.3$ – high probability of early PsA, justifying the initiation of specific treatment and early therapeutic intervention.

Model validation and clinical applicability

Retrospective validation of the model on the study cohort showed a sensitivity of 89% and a specificity of 84% for detecting early PsA. Comparison with subjective evaluations by rheumatologists demonstrated a high correlation ($r = 0.91$, $p < 0.001$), confirming the robustness of the model.

Example calculation for a hypothetical patient

- *Clinical parameters:* tender joint count (C1) = 5; morning stiffness duration (C2) = 35 minutes; swollen joint count (C3) = 3; presence of enthesitis (C4) = 1 (yes); presence of dactylitis (C5) = 1 (yes).
- *Laboratory markers:* ESR (L1) = 40 mm/h; CRP (L2) = 50 mg/L.

Step 1: Compute the Clinical Index (ϕC)

The clinical score is calculated using the formula:

$$\begin{aligned}\varphi C &= \frac{0.426 \times 5 + 0.567 \times 35 + 0.601 \times 3 + 0.645 \times 1 + 0.698 \times 1}{5} \\ &= \frac{2.13 + 19.845 + 1.803 + 0.645 + 0.698}{5} = \frac{25.121}{5} = 5.024\end{aligned}$$

Step 2: Compute the Laboratory Index (φL)

The laboratory score is calculated using:

$$\varphi L = \frac{0.084 \times 40 + 0.123 \times 50}{2} = \frac{3.36 + 6.15}{2} = \frac{9.51}{2} = 4.755$$

Step 3: Compute the Final Prediction Index (φAPs)

The final Psoriatic Arthritis Prediction Index is calculated using formula, where $W_C=0.55$ and $W_L=0.45$:

$$\varphi APs = 0.55 \times 5.024 + 0.45 \times 4.755 = 2.7632 + 2.13975 = 4.90295$$

Step 4: Interpretation of φAPs

Since the computed $\varphi APs=4.90$, this patient has a very high probability of early PsA, suggesting the need for immediate clinical evaluation and therapeutic intervention.

Discussion

The importance of early diagnosis of psoriatic arthritis

PsA is a systemic inflammatory disease characterized by a heterogeneous and, in many cases, unpredictable progression.⁴ Traditionally, early diagnosis has been a major challenge due to the absence of pathognomonic biomarkers and the variability of clinical presentations.⁶ Our study confirms that early identification of PsA is essential to prevent irreversible joint damage and to initiate appropriate therapy at an early stage, which can significantly improve long-term prognosis.

The data obtained in this research emphasize that in the early phase of PsA, specific clinical and biological changes occur, which may serve as early predictors of disease progression. We highlighted that enthesitis and dactylitis are the most distinctive manifestations of early PsA, with high diagnostic value, a finding that is also supported by existing

literature.^{7,10,11} This suggests that periarticular inflammation ⁷plays a crucial role in disease onset and could be one of the initial pathogenic factors preceding the diffuse synovial involvement characteristic of later stages.¹⁹

Distinctive clinical manifestations in early and late psA

Our results indicate that arthralgia, morning stiffness, and enthesitis were the most frequent symptoms in the preclinical period, with a ²⁸significantly higher prevalence in the early PsA group compared to PsO ($p < 0.001$). This supports the hypothesis proposed in the literature that periarticular inflammatory processes appear earlier than extensive synovial lesions.^{13,18}

Moreover, in early PsA, we observed a distinct distribution of enthesitis, with predominant involvement ³⁹of the Achilles tendon (80%), plantar fascia (72%), and humeral epicondyles (68%), whereas in PsO, enthesitis presented a more nonspecific and less severe distribution.

Additionally, the TJC and SJC were significantly lower in early PsA compared to PsO. This suggests that disease progression is characterized by the expansion of the inflammatory process to an increasing number of joints, justifying the need for close monitoring of patients with early oligoarticular forms to detect potential changes in disease pattern, which is typical of PsA.^{8,16}

The role of inflammatory biomarkers in differentiating early PsA and PsO

Laboratory parameters showed significant ¹differences between the two patient groups, reinforcing the hypothesis that early PsA is characterized by a more active inflammatory status. Patients in this group ¹had significantly higher levels of ESR (37.8 ± 2.4 mm/h) and CRP (36.25 ± 2.23 mg/L) compared to those with psoriasis without arthritis ($ESR = 15.2 \pm 2.1$ mm/h, $CRP = 8.12 \pm 3.14$ mg/L; $p < 0.01$). ⁴⁴This indicates a heightened systemic inflammatory response in the ²⁶early stages of the disease, which may justify the more aggressive use of disease-modifying anti-rheumatic drugs (DMARDs) at this stage. In the literature, it has been demonstrated that increased CRP levels in early PsA correlate with the activation of inflammatory cells and the

production of proinflammatory cytokines such as $\text{TNF-}\alpha$, IL-17, and IL-23.^{4,7,17} The decrease in CRP levels in psoriasis without arthritis suggests a lack of systemic inflammation, confirming that musculoskeletal involvement ¹ plays a crucial role in driving inflammatory activity in PsA.⁴ Furthermore, the observed differences in ESR ¹ and CRP levels between the two groups emphasize the importance of these biomarkers in differentiating early PsA from PsO, providing useful insights ¹ for early diagnosis and targeted treatment strategies.

Interpretation of the mathematical model and its clinical implications

One of the most significant outcomes of our study is the development and validation of an integrated mathematical model that combines clinical and laboratory indicators to differentiate early PsA from PsO. The model was constructed using multiple regression analysis and incorporated the most diagnostically relevant data:

- Clinical index (ϕC) – based on dactylitis, enthesitis, morning stiffness, TJC and SJC.
- Laboratory index (ϕL) – based on ESR and CRP levels.
- Composite index (ϕAPs) – derived from the weighting of clinical and laboratory indices, using coefficients optimized through logistic regression.

Retrospective validation of the model ⁷ demonstrated a sensitivity of 89% and a specificity of 84%, suggesting high reliability in identifying patients with early PsA. Additionally, ROC curve analysis confirmed that ϕAPs values ≥ 2.3 are strongly predictive of early PsA, while values below 1.8 largely exclude the diagnosis.

These results are clinically relevant as they allow for patient risk stratification and facilitate more objective therapeutic decision-making. Furthermore, applying this model in rheumatology practice could contribute to reducing diagnostic delays, a recognized issue in PsA management.

Study limitations

Although the obtained results support the validity of the proposed model, certain limitations must be considered. First, the study was conducted on a relatively small sample,

which may limit the generalizability of the results to a broader population. Additionally, asymptomatic patients or those with nonspecific manifestations were not included, which may impact the model's applicability to atypical PsA cases.

Second, while our model has proven robust, longitudinal patient evaluation is necessary to determine its predictive capacity for long-term disease progression. External validation in independent cohorts is also an essential step for confirming the model's reliability and reproducibility.

Future directions and clinical implications

Our study highlights the importance of integrating clinical and biological data into a mathematical model for the early diagnosis of PsA. This approach may contribute to optimizing treatment strategies, enabling the early initiation of DMARDs in patients at high risk of disease progression. In the future, combining this model with molecular biomarkers and advanced imaging data (e.g., functional MRI, artificial intelligence applied to image analysis) could further improve diagnostic accuracy.

Thus, our integrative mathematical model provides a reliable and reproducible method for early PsA diagnosis, combining clinical and laboratory parameters into an objective and clinically applicable algorithm. Validation of this model in multicenter studies is necessary to confirm its utility in current rheumatology practice.

In conclusion, this study demonstrates the importance of early diagnosis of PsA by integrating clinical and laboratory data into a predictive mathematical model. Our analysis highlighted that dactylitis, enthesitis, and morning stiffness are essential clinical markers in the early stages of the disease, while elevated ESR and CRP levels reflect increased systemic inflammatory activity. The proposed mathematical model combines these parameters into a composite index (ϕ APs), with a sensitivity of 89% and a specificity of 84% for identifying early PsA. A threshold of ϕ APs ≥ 2.3 indicates a high probability of disease, suggesting the need for immediate therapeutic intervention.

The results emphasize the importance of an integrated approach to early PsA diagnosis, contributing to better patient stratification and timely treatment initiation. Although the model has high accuracy, external validation on independent cohorts is essential to confirm its clinical applicability. In the future, combining this model with molecular biomarkers and advanced

Key Points

- Early diagnosis of psoriatic arthritis (PsA) is critical for preventing joint damage and disability.
- This study developed a predictive composite index incorporating clinical, laboratory, and imaging parameters to differentiate early PsA from cutaneous psoriasis (PsO) without musculoskeletal involvement.
- The model demonstrated high sensitivity (89%) and specificity (84%) in identifying early PsA, supporting its potential role in clinical decision-making.
- Enthesitis, dactylitis, morning stiffness, and inflammatory markers (ESR, CRP) were the most informative variables for early PsA detection.
- Further validation in multicenter cohorts is needed to confirm the model's applicability in rheumatology practice.

Author contributions

ER, VC, and LG conceived and designed the study. ER, VC, LC, OB, and MH performed data analysis and interpretation. ER and VC drafted the manuscript. All authors critically revised the manuscript for intellectual content, approved the final version, and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare no conflicts of interest.

Funding

This study received no external funding.

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Nicolae Testemițanu State University of Medicine and Pharmacy, Moldova (Approval No. 21, Dec. 201X). ¹³ Written informed consent was obtained from all participants prior to their inclusion in the study.

References

1. Alinaghi F, Calov M, Kristensen LE, *et al.* Prevalence of Psoriatic arthritis in patients with psoriasis: A systematic review and meta-analysis of observational and clinical studies. *J Am Acad Dermatol* 2019;80:251–65. doi:10.1016/j.jaad.2018.06.027
2. Gladman DD, Antoni C, Mease P, *et al.* Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64:ii14–7. doi:10.1136/ard.2004.032482
3. Perez-Chada LM, Haberman RH, Chandran V, *et al.* Consensus terminology for Preclinical phases of Psoriatic arthritis for use in research studies: results from a Delphi consensus study. *Nat Rev Rheumatol* 2021;17:238–43. doi:10.1038/s41584-021-00578-2
4. Eder L, Polachek A, Rosen CF, *et al.* 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;69:622–9. doi:10.1002/art.39973
5. Zabotti A, McGonagle DG, Giovannini I, *et al.* Transition phase towards Psoriatic arthritis: clinical and ultrasonographic Characterisation of Psoriatic arthralgia. *RMD Open* 2019;5:e001067. doi:10.1136/rmdopen-2019-001067
6. Zabotti A, Tinazzi I, Aydin SZ, *et al.* From psoriasis to Psoriatic arthritis: insights from imaging on the transition to Psoriatic arthritis and implications for arthritis prevention. *Curr Rheumatol Rep* 2020;22:24. doi:10.1007/s11926-020-00891-x

7. Faustini F, Simon D, Oliveira I, *et al.* Subclinical joint inflammation in patients with psoriasis without concomitant Psoriatic arthritis: a cross-sectional and longitudinal analysis. *Ann Rheum Dis* 2016;75:2068–74. [doi:10.1136/annrheumdis-2015-208821](https://doi.org/10.1136/annrheumdis-2015-208821)
8. Belman S, Walsh JA, Carroll C, *et al.* Psoriasis characteristics for the early detection of Psoriatic arthritis. *J Rheumatol* 2021;48:1559–65. [doi:10.3899/jrheum.201123](https://doi.org/10.3899/jrheum.201123)
9. Scher JU, Ogdie A, Merola JF, *et al.* Preventing Psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition. *Nat Rev Rheumatol* 2019;15:153–66. [doi:10.1038/s41584-019-0175-0](https://doi.org/10.1038/s41584-019-0175-0)
10. Simon D, Tascilar K, Kleyer A, *et al.* Association of structural Enteseal lesions with an increased risk of progression from psoriasis to Psoriatic arthritis. *Arthritis Rheumatol* 2022;74:253–62. [doi:10.1002/art.41239](https://doi.org/10.1002/art.41239)
11. Aydin SZ, Bridgewood C, Zabotti A, *et al.* The transition from Enthesis physiological responses in health to aberrant responses that underpin Spondyloarthritis mechanisms. *Curr Opin Rheumatol* 2021;33:64–73. [doi:10.1097/BOR.0000000000000768](https://doi.org/10.1097/BOR.0000000000000768)
12. Raza K, Saber TP, Kvien TK, *et al.* Timing the therapeutic window of opportunity in early rheumatoid arthritis: proposal for definitions of disease duration in clinical trials. *Ann Rheum Dis* 2012;71:1921–3. [doi:10.1136/annrheumdis-2012-201893](https://doi.org/10.1136/annrheumdis-2012-201893)
13. Zabotti A, De Lucia O, Sakellariou G, *et al.* Predictors, risk factors, and incidence rates of Psoriatic arthritis development in psoriasis patients: A systematic literature review and meta-analysis. *Rheumatol Ther* 2021;8:1519–34. [doi:10.1007/s40744-021-00378-w](https://doi.org/10.1007/s40744-021-00378-w)
14. Eder L, Haddad A, Rosen CF, *et al.* The incidence and risk factors for Psoriatic arthritis in patients with psoriasis: A prospective cohort study. *Arthritis & Rheumatology* 2016;68:915–23. [doi:10.1002/art.39494](https://doi.org/10.1002/art.39494)
15. Myers A, Kay LJ, Lynch SA, *et al.* Recurrence risk for psoriasis and Psoriatic arthritis within Sibships. *Rheumatology* (Oxford) 2005;44:773–6. [doi:10.1093/rheumatology/keh589](https://doi.org/10.1093/rheumatology/keh589)

16. Green A, Shaddick G, Charlton R, *et al.* Modifiable risk factors and the development of Psoriatic arthritis in people with psoriasis. *Br J Dermatol* 2020;182:714–20. doi:10.1111/bjd.18227 Available: <https://onlinelibrary.wiley.com/toc/13652133/182/3>
17. McGonagle DG, Zabotti A, Watad A, *et al.* Intercepting Psoriatic arthritis in patients with psoriasis: buy one get one free? *Ann rheum DIS Ann Rheum Dis* 2022;81:7–10. doi:10.1136/annrheumdis-2021-221255
18. Wilson FC, Icen M, Crowson CS, *et al.* Incidence and clinical predictors of Psoriatic arthritis in patients with psoriasis: a population-based study. *Arthritis Rheum* 2009;61:233–9. doi:10.1002/art.24172
19. Mulder MLM, van Hal TW, Wenink MH, *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. doi:10.1186/s13075-021-02545-4
20. D'Angelo S, Mennillo GA, Cutro MS, *et al.* Sensitivity of the classification of Psoriatic arthritis criteria in early Psoriatic arthritis. *J Rheumatol* 2009;36:368–70. doi:10.3899/jrheum.080596
21. Aletaha D. The undifferentiated arthritis dilemma: the story continues. *Nat Rev Rheumatol* 2022;18:189–90. doi:10.1038/s41584-022-00762-y
22. Elnady B, El Shaarawy NK, Dawoud NM, *et al.* Subclinical Synovitis and Enthesitis in psoriasis patients and controls by Ultrasonography in Saudi Arabia; incidence of Psoriatic arthritis during two years. *Clin Rheumatol* 2019;38:1627–35. doi:10.1007/s10067-019-04445-0

Development of a Predictive Composite Index for early diagnosis of psoriatic arthritis

ORIGINALITY REPORT

17%	12%	13%	4%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	"2013 Annual Meeting Abstract Supplement", Arthritis & Rheumatism, 2013. Publication	3%
2	www.frontiersin.org Internet Source	1%
3	core.ac.uk Internet Source	1%
4	www.mdpi.com Internet Source	1%
5	www.researchsquare.com Internet Source	1%
6	www.researchgate.net Internet Source	1%
7	idoc.pub Internet Source	1%
8	Fabiola Atzeni, Elisabetta Gerratana, Ignazio Francesco Masala, Sara Bongiovanni et al. "Psoriatic Arthritis and Metabolic Syndrome: Is There a Role for Disease Modifying Anti-Rheumatic Drugs?", Frontiers in Medicine, 2021 Publication	<1%
9	www.biomedscidirect.com Internet Source	<1%
10	portal.research.lu.se Internet Source	<1%

11

Internet Source

<1 %

12

arthritis-research.biomedcentral.com

Internet Source

<1 %

13

www.scipublications.com

Internet Source

<1 %

14

I Belinchón, L Salgado-Boquete, A López-Ferrer, M Ferran et al. "Dermatologists' Role in the Early Diagnosis of Psoriatic Arthritis: Expert Recommendations", Actas Dermo-Sifiliográficas (English Edition), 2020

Publication

<1 %

15

A. Mathieu. "The psoriatic arthritis cost evaluation study: a cost-of-illness study on tumour necrosis factor inhibitors in psoriatic arthritis patients with inadequate response to conventional therapy", Rheumatology, 08/13/2008

Publication

<1 %

16

Akio Morita, Tetsuro Sameshima, Shigeo Sora, Toshikazu Kimura et al. "Development of a New Compact Intraoperative Magnetic Resonance Imaging System: Concept and Initial Experience", Operative Neurosurgery, 2014

Publication

<1 %

17

Otto Olivas-Vergara, Lina Martínez-Estupiñán, Fredeswinda Romero-Bueno, Olga Sánchez-Pernaute et al. "Value of ultrasound-assessed dactylitis in the early diagnosis of psoriatic arthritis", Seminars in Arthritis and Rheumatism, 2024

Publication

<1 %

18

Submitted to University of Exeter

Student Paper

<1 %

19	Internet Source	<1 %
20	pubmed.ncbi.nlm.nih.gov Internet Source	<1 %
21	www.healio.com Internet Source	<1 %
22	Panpan Liu, Yehong Kuang, Li Ye, Cong Peng, Wangqing Chen, Minxue Shen, Mi Zhang, Wu Zhu, Chengzhi Lv, Xiang Chen. "Predicting the Risk of Psoriatic Arthritis in Plaque Psoriasis Patients: Development and Assessment of a New Predictive Nomogram", Frontiers in Immunology, 2022 Publication	<1 %
23	Submitted to University of New England Student Paper	<1 %
24	ard.bmj.com Internet Source	<1 %
25	bloodjournal.ru Internet Source	<1 %
26	www.guidelinesinpractice.co.uk Internet Source	<1 %
27	Xuejiao Liu, Yue Meng, Bin Fu, Haoru Song, Bing Gu, Ying Zhang, Haojie Lu. "GlycoPro: A High-Throughput Sample-Processing Platform for Multi-Glycosylation-Omics Analysis", Engineering, 2025 Publication	<1 %
28	turkjpediatr.org Internet Source	<1 %
29	www.tandfonline.com Internet Source	<1 %
30	E. Daudén, S. Castañeda, C. Suárez, J. García-Campayo et al. "Integrated Approach to	<1 %

Comorbidity in Patients With Psoriasis", Actas Dermo-Sifiliográficas (English Edition), 2012

Publication

-
- | | | |
|---|--|----------------|
| <div style="background-color: #8B4513; color: white; padding: 2px 5px; display: inline-block;">31</div> | Submitted to University of Oxford
<small>Student Paper</small> | <1 % |
|---|--|----------------|
-
- | | | |
|---|--|----------------|
| <div style="background-color: #0056b3; color: white; padding: 2px 5px; display: inline-block;">32</div> | redsaludfronteriza.org.mx
<small>Internet Source</small> | <1 % |
|---|--|----------------|
-
- | | | |
|---|---|----------------|
| <div style="background-color: #800080; color: white; padding: 2px 5px; display: inline-block;">33</div> | topsecretapiaccess.dovepress.com
<small>Internet Source</small> | <1 % |
|---|---|----------------|
-
- | | | |
|---|---|----------------|
| <div style="background-color: #6b8e23; color: white; padding: 2px 5px; display: inline-block;">34</div> | "Connective Tissue Disease", Springer Science and Business Media LLC, 2024
<small>Publication</small> | <1 % |
|---|---|----------------|
-
- | | | |
|---|--|----------------|
| <div style="background-color: #000080; color: white; padding: 2px 5px; display: inline-block;">35</div> | Danielle Bar, Merav Lidar, Sharon Baum, Aviv Barzilai, Felix Pavlotsky, Amit Druyan. "Early Methotrexate Treatment For Psoriatic Arthritis Prevention in Psoriasis Patients – a retrospective cohort study", Joint Bone Spine, 2024
<small>Publication</small> | <1 % |
|---|--|----------------|
-
- | | | |
|---|--|----------------|
| <div style="background-color: #0070c0; color: white; padding: 2px 5px; display: inline-block;">36</div> | Mathew, Ashish J, Laura C Coates, Debashish Danda, and Philip G Conaghan. "Psoriatic arthritis: Lessons from imaging studies and implications for therapy", Expert Review of Clinical Immunology, 2016.
<small>Publication</small> | <1 % |
|---|--|----------------|
-
- | | | |
|---|--|----------------|
| <div style="background-color: #ff0000; color: white; padding: 2px 5px; display: inline-block;">37</div> | Ranran Yao, An-Ping Huo, Yuan Jia, Yin Su. "Psoriatic arthritis: Overcoming the obstacles of early diagnosis and optimal management", International Journal of Rheumatic Diseases, 2024
<small>Publication</small> | <1 % |
|---|--|----------------|
-
- | | | |
|---|--|----------------|
| <div style="background-color: #ff00ff; color: white; padding: 2px 5px; display: inline-block;">38</div> | docshare.tips
<small>Internet Source</small> | <1 % |
|---|--|----------------|
-
- | | | |
|---|--|----------------|
| <div style="background-color: #8000ff; color: white; padding: 2px 5px; display: inline-block;">39</div> | sok.helsebiblioteket.no
<small>Internet Source</small> | <1 % |
|---|--|----------------|
-

40	web.archive.org Internet Source	<1 %
41	www.biomedcentral.com Internet Source	<1 %
42	www.diva-portal.org Internet Source	<1 %
43	www.jrheum.org Internet Source	<1 %
44	www.termedia.pl Internet Source	<1 %
45	Davis, J.C.. "Insights Into the Pathology and Treatment of Spondyloarthritis: From the Bench to the Clinic", Seminars in Arthritis and Rheumatism, 200810 Publication	<1 %
46	Fabian Proft, Susanne Lüders, Theresa Hunter, Gustavo Luna et al. "Early identification of axial psoriatic arthritis among patients with psoriasis: a prospective multicentre study", Annals of the Rheumatic Diseases, 2022 Publication	<1 %
47	Psoriatic Arthritis and Psoriasis, 2016. Publication	<1 %
48	Ashish J. Mathew, Mikkel Østergaard. "Magnetic Resonance Imaging of Enthesitis in Spondyloarthritis, Including Psoriatic Arthritis —Status and Recent Advances", Frontiers in Medicine, 2020 Publication	<1 %