Missing early psoriatic arthritis means irreversible joint damage

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> Psoriasis affects millions, but for a significant subset, the skin manifestations are merely the visible tip of an inflammatory iceberg. Psoriatic arthritis (PsA), a debilitating inflammatory joint disease, often follows psoriasis, yet its early detection remains a clinical challenge. Identifying these patients before irreversible joint damage occurs is a critical unmet need.

KEY TAKEAWAYS

- The Pivot: A model combining the Psoriasis Epidemiology Screening Tool (PEST) with the Systemic Immune-Inflammation Index (SII) and CALLY index values may predict PsA development in psoriasis patients.
- The Data: The PEST questionnaire demonstrated a sensitivity of 83.7% and specificity of 74.2% for detecting PsA in a longitudinal registry.
- The Action: Clinicians should consider integrating validated screening tools like PEST into routine psoriasis patient assessments, particularly when evaluating inflammatory markers or CALLY index values.

Psoriasis, a chronic inflammatory skin condition, affects approximately 2-3% of the global population. While its dermatological impact is well-recognised, the systemic nature of the disease often leads to comorbidities, with psoriatic arthritis (PsA) being one of the most significant. PsA develops in up to 30% of psoriasis patients, frequently manifesting years after the initial skin symptoms. Early diagnosis and intervention are crucial to prevent progressive joint damage and preserve physical function, but the path from psoriasis to PsA is often subtle and difficult to predict. This diagnostic lag represents a substantial clinical burden, as many patients experience significant joint erosion before receiving a PsA diagnosis.

The Psoriasis Epidemiology Screening Tool (PEST) is a 5-item questionnaire specifically designed to help identify psoriasis patients who may have co-existing PsA. This tool aims to bridge the diagnostic gap by providing a simple, quick method for clinicians to assess for arthritic symptoms. The PURE registry, a prospective, observational, 5-year study, investigated the longitudinal performance of the PEST questionnaire in a diverse cohort of patients from Canada and Latin America. This registry enrolled a broad spectrum of psoriasis patients, including those with varying disease severities and durations, providing a real-world context for evaluating PEST's utility. The primary objective was to assess PEST's ability to identify PsA over time, tracking changes in patient symptoms and diagnoses.1

Evaluating PEST's Performance in a Longitudinal Cohort

Beecker, Albrecht, and Dei-Cas conducted a comprehensive analysis of the PEST questionnaire's longitudinal performance within the PURE registry.1 This prospective, observational study followed patients for five years, allowing for a dynamic assessment of PEST's predictive capabilities. The PURE registry included 1,540 patients with psoriasis, of whom 462 (30%) had a baseline diagnosis of PsA. The remaining 1,078 patients were initially diagnosed with psoriasis alone, forming the cohort for incident PsA detection. Over the five-year follow-up, 128 patients (11.9% of the psoriasis-only cohort) developed new-onset PsA, confirmed by a rheumatologist. The PEST questionnaire was administered annually to all participants, with a score of 3 or higher considered positive for potential PsA.1

The PEST questionnaire demonstrated a sensitivity of 83.7% (95% CI, 76.8-89.1) and a specificity of 74.2% (95% CI, 71.3-77.0) for detecting PsA in the PURE registry cohort. Its positive predictive value (PPV) was 31.5%, and its negative predictive value (NPV) was 96.8%. This high NPV suggests that a negative PEST score reliably indicates a low likelihood of PsA, which is clinically useful for ruling out the condition. The area under the receiver operating characteristic curve (AUC) for PEST was 0.79, indicating a reasonable ability to discriminate between patients with and without PsA.1

The investigators also examined the individual items of the PEST questionnaire. They found that questions related to joint swelling and morning stiffness were particularly strong indicators of PsA development. Patients who reported joint swelling in two or more joints had an odds ratio (OR) of 4.5 (95% CI, 3.1-6.5; P<.001) for developing PsA, while those with morning stiffness lasting more than 30 minutes had an OR of 3.2 (95% CI, 2.2-4.7; P<.001). These specific symptoms, when present, should prompt a more thorough rheumatological evaluation.1

Integrating Inflammatory Markers and Disease Activity Indices

Beyond the PEST questionnaire, other biomarkers and clinical indices offer additional insights into PsA risk and disease activity. Yildiz and Limon explored the CALLY index, a composite score reflecting patient-reported outcomes, in a retrospective cohort study.2 Their analysis, though focused on established PsA, revealed that lower CALLY index values were associated with higher disease activity. Specifically, patients with a CALLY index below 15 had a 2.8-fold higher likelihood of having moderate-to-high disease activity (OR 2.8; 95% CI, 1.9-4.1; P=.003) compared to those with higher CALLY scores. This suggests that while PEST screens for presence, CALLY might help quantify the severity of arthritic symptoms.2

The CALLY index, which incorporates measures like pain, functional impairment, and global assessment, provides a patient-centric view of disease impact. In the context of predicting PsA, a persistently low CALLY index in a psoriasis patient, even before overt PsA diagnosis, could signal underlying inflammatory processes that warrant closer monitoring. The study by Yildiz and Limon included 320 patients with established PsA, demonstrating the index's utility in a cohort where the disease was already present. While not directly a predictive tool for incident PsA, its association with disease activity offers a complementary perspective for clinicians managing psoriasis patients at risk.2

Trovato and colleagues investigated the Systemic Immune-Inflammation Index (SII) as a predictive biomarker for therapeutic response in psoriasis.3 Although their study focused on treatment response rather than PsA prediction, the SII, calculated from peripheral blood platelet, neutrophil, and lymphocyte counts, reflects systemic inflammation. Higher baseline SII values were associated with a poorer response to anti-TNF, anti-IL-17, and anti-IL-23 agents in psoriasis patients. For instance, patients with a baseline SII above 700 had a 38% lower likelihood of achieving PASI 75 at 12 weeks (OR 0.62; 95% CI, 0.45-0.85; P=.002) compared to those with lower SII values. This suggests that a heightened inflammatory state, as indicated by SII, could also predispose patients to developing PsA.3

The SII, as a readily available and inexpensive biomarker, offers a potential avenue for risk stratification. A psoriasis patient with a high SII might not only respond less effectively to systemic therapies but also carry an elevated systemic inflammatory burden that could accelerate the development of PsA. The Trovato study, a retrospective comparative analysis, included 580 psoriasis patients undergoing systemic treatment. While the direct link to PsA incidence was not the primary endpoint, the underlying inflammatory mechanisms are shared.3

Building a Predictive Model for PsA

Combining these disparate pieces of evidence, a more robust predictive model for PsA in psoriasis patients begins to emerge. The PEST questionnaire serves as the initial, easily administered screening tool. Its high NPV makes it effective for ruling out PsA in many patients, reducing unnecessary referrals. But for those with a positive PEST score, further stratification becomes essential. The Oxford Handbook of Rheumatology provides comprehensive guidance on these complex diagnostic pathways.

A patient with psoriasis who screens positive on PEST, particularly with symptoms like joint swelling or prolonged morning stiffness, should then be evaluated for systemic inflammatory markers. A persistently elevated SII, as described by Trovato and colleagues, could indicate a higher systemic inflammatory load, potentially increasing the risk of PsA development or progression. This objective biomarker complements the subjective patient-reported symptoms captured by PEST.3

But the CALLY index, while primarily a measure of disease activity in established PsA, could also play a role in monitoring high-risk psoriasis patients. A declining CALLY index, even in the absence of a formal PsA diagnosis, might signal worsening subclinical arthritic symptoms or functional impairment. This would prompt a more aggressive diagnostic workup, including imaging studies or referral to a rheumatologist. The integration of these three tools (PEST, SII, and CALLY) creates a multi-modal approach to PsA prediction, moving beyond a single questionnaire to incorporate both patient experience and objective inflammatory markers.1,2,3

Where the Data Falls Short

The PURE registry, while longitudinal and observational, relied on annual PEST assessments. This frequency might miss some rapidly progressing cases of PsA, as symptoms can fluctuate. The confirmation of PsA diagnosis by a rheumatologist is a strength, but the subjective nature of some PEST questions introduces potential for recall bias. The study population, drawn from Canada and Latin America, offers some diversity, but generalisability to other ethnic groups or healthcare systems requires further validation.1

The CALLY index study was retrospective and focused on established PsA, limiting its direct applicability to predicting incident disease. Its association with disease activity is clear, but its role as a pre-diagnostic marker needs prospective validation. Similarly, the SII study examined therapeutic response in psoriasis, not PsA incidence. While systemic inflammation is a shared pathway, extrapolating its predictive value for PsA requires dedicated research. The retrospective design of both the CALLY and SII studies means they cannot establish causality, only associations.2,3

The lack of a unified, prospectively validated model combining PEST, SII, and CALLY is an obvious caveat. Each tool offers a piece of the puzzle, but their synergistic predictive power has not been formally tested in a single, large-scale trial. The optimal cut-off points for SII and CALLY in a predictive context also remain to be defined. The cost-effectiveness

of routine SII and CALLY monitoring in all psoriasis patients at risk for PsA also requires economic evaluation. These are all areas where further research is needed to refine and validate a comprehensive predictive strategy.

CLINICAL IMPLICATIONS

The PEST questionnaire offers a practical, low-cost method for GPs and dermatologists to screen for psoriatic arthritis in their psoriasis patients. Its high negative predictive value means a negative score can reassure both clinician and patient, reducing unnecessary specialist referrals. But a positive score, particularly with specific symptoms like joint swelling, demands further investigation, not just a shrug.

Integrating objective inflammatory markers like the Systemic Immune-Inflammation Index (SII) could refine this screening process. While not a direct PsA predictor, an elevated SII signals a heightened inflammatory state that warrants closer attention. This readily available blood test could flag patients who might benefit from earlier rheumatology consultation, potentially before irreversible joint damage occurs.

The CALLY index, though primarily a measure of disease activity, provides a patient-reported outcome that could complement PEST and SII. A declining CALLY score in a psoriasis patient, even without a formal PsA diagnosis, should prompt a re-evaluation of their overall inflammatory burden. This multi-modal approach moves beyond a single screening tool, offering a more comprehensive risk assessment for a condition that often presents subtly.

The challenge now lies in validating a combined model prospectively and establishing clear clinical pathways for patients identified as high-risk. Without this, even the most sensitive screening tools remain just that: tools, not solutions. The goal is not just to identify PsA, but to intervene effectively and early.

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