



Clinical Study

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Inflammatory Markers as Predictors of Joint Damage Progression in Psoriatic Arthritis

Rowe S^{1*}, Lindo W² and Prescod R³

¹Department of Translational Medicine, Port of Spain Center for Rheumatology, Jamaica Scopus Author ID: 57597737218 Email: shanice.rowe@port.edu
ORCID: <https://orcid.org/9756-8779-6986-0354>

²Department of Biomedical Research, Nassau Center for Joint Health, Guyana Scopus Author ID: 57957633556 Email: wesley.lindo@nassau.edu
ORCID: <https://orcid.org/3643-3358-1655-1527>

³Department of Clinical Research, Nassau Center for Joint Health, Guyana Scopus Author ID: 57996286016 Email: renee.prescod@nassau.edu
ORCID: <https://orcid.org/1402-2491-2864-0103>

***Correspondence to:** Shanice Rowe, Department of Translational Medicine, Port of Spain Center for Rheumatology, Jamaica Scopus Author ID: 57597737218 Email: shanice.rowe@port.edu

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Abstract

Psoriatic arthritis (PsA) can produce irreversible joint damage even in patients whose clinical assessment appears reassuring, motivating longstanding interest in whether routinely measured inflammatory markers can flag those at highest structural risk. This article synthesizes the literature on C-reactive protein (CRP), erythrocyte sedimentation rate, and a range of soluble and imaging-based inflammatory biomarkers as predictors of joint damage progression in PsA. Across randomized trial subanalyses and observational cohorts spanning different treatment eras, elevated baseline CRP consistently and independently associates with subsequent radiographic progression, though it explains only part of the variance and adds to, rather than replaces, clinical joint assessment. Soluble biomarker panels and chemokines such as CXCL10 improve discrimination between psoriatic arthritis and psoriasis alone but remain short of validated tools for predicting structural progression specifically. Musculoskeletal ultrasound and magnetic resonance imaging reveal substantial subclinical synovial and enthesal inflammation undetected by serum markers or examination, exposing a gap between what CRP captures and the true inflammatory burden driving damage in some patients. We conclude that inflammatory markers are best used as one input within multidomain, composite assessment, as current treatment guidelines already recommend, while a validated, individual-level model integrating serum and imaging biomarkers into a single structural-risk estimate remains an open research priority.

Keywords: psoriatic arthritis; C-reactive protein; radiographic progression; inflammatory biomarkers; joint damage

1. Introduction

Psoriatic arthritis (PsA) is often introduced to trainees as a disease that "looks milder than rheumatoid arthritis on paper and behaves worse in practice." That framing captures something real: a meaningful fraction of patients accrue irreversible joint damage — erosions, joint space narrowing, and in some cases ankylosis — well before that damage is clinically obvious, and radiographic progression can occur even in patients who look reasonably well controlled by tender and swollen joint counts alone [1,2]. The consequence is a persistent clinical puzzle: which patients, at first presentation or during otherwise unremarkable follow-up, are quietly building toward structural damage that will cost them function, and which patients can be watched more conservatively? Inflammatory markers — the humble C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) that clinicians order almost reflexively, alongside a growing menu of soluble cytokines, chemokines, and imaging-based measures of subclinical synovitis — sit at the center of that puzzle. They are cheap, familiar, and at least in principle biologically connected to the process that erodes cartilage and bone. Whether they are actually good predictors of joint damage progression, and under what conditions, is a narrower and more interesting question than it first appears.

This article synthesizes what the published literature says about inflammatory markers as predictors of radiographic and structural progression in PsA. It is not a report of new data; it is an attempt to lay the relevant studies — longitudinal cohorts, randomized trial subanalyses, biomarker-discovery work, and imaging studies — next to each other and ask what they collectively support, where they disagree, and where the evidence runs out. We begin with the disease burden that makes this question worth asking, move through the pathobiology that connects inflammation to structural damage, examine acute-phase reactants and biomarker panels in turn, consider what imaging adds when serum markers are ambiguous, and close with where inflammatory-marker-guided prognostication sits relative to treat-to-target strategy and where it still falls short.

2. Psoriatic Arthritis: Disease Burden and the Case for Prognostic Biomarkers

PsA affects a substantial minority of people with

psoriasis — estimates in the epidemiological literature commonly place the proportion in the range of roughly one in five to one in three psoriasis patients over a lifetime, though methodology and case ascertainment vary considerably across studies, and the disease's heterogeneous presentation makes precise, generalizable estimates difficult to pin down [3]. Unlike rheumatoid arthritis, PsA involves a genuinely pleiotropic set of domains — peripheral arthritis, axial disease, enthesitis, dactylitis, and skin and nail disease — and a patient can have substantial structural risk in one domain while looking unremarkable in another [1,2]. This heterogeneity is precisely why prognostic biomarkers matter clinically: a treat-to-target strategy applied uniformly to all patients risks both undertreating those on a trajectory toward damage and overtreating those who would have done well regardless.

The case for inflammatory-marker-based prognostication rests on a simple premise borrowed from rheumatoid arthritis: if systemic and local inflammation is mechanistically upstream of the bone and cartilage destruction seen on radiographs, then markers of that inflammation, measured early, should carry some predictive signal for who will progress. The complication, well documented in the PsA literature, is that structural damage in PsA does not track cleanly with the same inflammatory burden that drives progression in rheumatoid arthritis; PsA joint damage has a bone-formation component (periostitis, enthesophytes, ankylosis) alongside erosive bone loss, reflecting a biology that is not simply "rheumatoid arthritis with psoriasis" [1,4]. That divergence is why inflammatory markers validated as prognostic in rheumatoid arthritis cannot simply be assumed to transfer, and why PsA-specific evidence is needed.

Diagnostic Context

Before inflammatory markers can be used prognostically, patients have to be correctly classified as having PsA in the first place, and it is worth noting how imperfect acute-phase reactants are even for that more basic task. The CASPAR (Classification Criteria for Psoriatic Arthritis) study, developed from a large international case-control dataset, deliberately included CRP only as a minor, non-mandatory criterion — one point among several — precisely because elevated CRP is neither sensitive nor specific enough on its own to distinguish PsA from other inflammatory or

non-inflammatory joint diseases; the full CASPAR criteria set achieved a sensitivity of 91.4% and specificity of 98.7% only by combining multiple weighted clinical, radiographic, and serological features, not by relying on inflammatory markers in isolation [5]. That detail matters for the rest of this synthesis: if CRP is a weak diagnostic feature, its value has to be argued for separately as a prognostic one, using longitudinal rather than cross-sectional evidence.

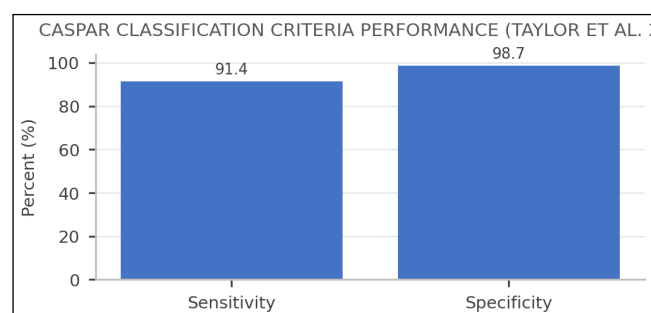


Figure 1: Sensitivity and specificity of the CASPAR classification criteria for psoriatic arthritis, as reported in the original large international case-control validation study. CRP is included only as a minor, non-mandatory item within the full weighted criteria set, illustrating why acute-phase reactants alone are insufficient for diagnosis and must instead be evaluated as one input among several, a theme that recurs when the same markers are examined for their prognostic value in this article [5].

Why "Milder-Looking" Disease Still Damages Joints

Part of what makes PsA a difficult disease to risk-stratify is that its clinical severity and its structural severity are only loosely coupled. Patients can present with a handful of swollen joints, unremarkable global assessments, and near-normal inflammatory markers, and still be found on serial radiographs to have accrued new erosions over a year or two of follow-up; conversely, patients with dramatic skin disease and high subjective symptom burden do not automatically carry the highest structural risk [1,2]. This decoupling is exactly the gap that a good prognostic biomarker would need to close — identifying, among patients who look similar on routine clinical assessment, the subset whose disease biology is nonetheless tilted toward progressive joint destruction. Inflammatory markers are attractive candidates for that role primarily because they are already embedded in routine care: a CRP or ESR is drawn as a matter of course in most rheumatology visits, at negligible marginal cost, which means that if these markers carry real prognostic signal, that signal is available essentially for free, without new infrastructure or specialized testing. The question this article works through is how much of that signal is actually there, and how it should be weighted against the imaging- and biomarker-based alternatives that are

more expensive but, in some studies, more sensitive to the biology being measured.

3. Pathobiology of Joint Damage in Psoriatic Arthritis

Structural damage in PsA arises from a network of overlapping processes rather than a single inflammatory pathway. Synovial and enthesial inflammation, mediated substantially by the IL-23/IL-17 axis alongside TNF, drives osteoclast activation and bone erosion, while the same inflammatory milieu — somewhat paradoxically — also stimulates new bone formation at enthesal sites, producing the syndesmophytes, periostitis, and eventual ankylosis that distinguish PsA radiographs from those of rheumatoid arthritis [4,1]. Recent mechanistic reviews describe this as a tissue-specific balance between destructive and reparative signaling that appears to be regulated differently across the enthesis, synovium, and bone, with cytokine milieu, mechanical stress, and local growth factor signaling (including Wnt and BMP pathways) all implicated in tipping that balance toward net bone loss or net new bone formation in a given joint at a given time [4].

This dual biology has a direct implication for biomarker research: a single circulating marker of "inflammation" is unlikely to capture the full picture of structural risk, because erosive and osteoproliferative processes may be driven by overlapping but not identical signaling. It also explains why enthesal and synovial inflammation, which is often subclinical and difficult to detect by joint examination alone, has become such a focus of imaging-based biomarker work — a point taken up later in this article.

The Enthesis as an Initiating Site

A recurring theme in PsA pathobiology over the past two decades has been the primacy of the enthesis — the insertion site of tendon, ligament, or joint capsule into bone — as a site where inflammation may originate before spreading to adjacent synovium, a model sometimes called the "synovio-entheseal complex" [1,4]. If enthesitis genuinely precedes and drives synovitis in at least a subset of patients, then serum inflammatory markers, which largely reflect systemic and synovial inflammatory burden, may systematically under-detect early enthesal disease that nonetheless carries structural risk. This has motivated the imaging literature discussed later, which repeatedly finds subclinical

enthesitis and synovitis in patients who appear clinically quiescent and whose CRP is normal [6].

Bone Biology and the Limits of a Single Inflammatory Signal

It is worth dwelling further on why this dual erosive/osteoproliferative biology complicates the search for a single predictive marker. In diseases where structural damage is purely erosive, a marker tracking inflammatory burden has a comparatively simple job: higher marker, more inflammation, more erosion, in a roughly monotonic relationship. In PsA, the same inflammatory signaling that promotes osteoclast-mediated bone resorption at one site can, through mechanisms involving Wnt signaling antagonists like sclerostin and Dickkopf-1, promote osteoblast-mediated new bone formation at another, sometimes in the same patient at the same point in time [4]. A circulating marker like CRP, which reflects systemic hepatic acute-phase response rather than the local balance of these opposing signals, is therefore mechanistically better positioned to predict "how much structural change is likely to occur" in aggregate than to predict "what kind" of change — erosive, proliferative, or both — will occur at a specific joint. This distinction matters for how progression is measured and interpreted in the studies reviewed below: modified Sharp/van der Heijde scores sum erosion and joint space narrowing subscores, which can obscure heterogeneity in the underlying process even when the aggregate score shows a clear association with a given marker.

4. Acute-Phase Reactants: CRP and ESR as Predictors of Radiographic Progression

The most direct evidence on this article's central question comes from studies that explicitly relate baseline or longitudinal CRP (or ESR) to subsequent radiographic change, usually measured by a modified Sharp/van der Heijde score or an equivalent structural damage index.

A subanalysis of the ADEPT randomized controlled trial of adalimumab in PsA identified elevated baseline CRP as one of the strongest independent predictors of radiographic progression among the clinical and demographic variables examined, alongside other markers of disease severity such as higher baseline modified Sharp score and greater number of damaged joints; adalimumab treatment reduced the risk of

progression overall, with the clearest benefit seen in patients whose baseline inflammatory burden — reflected in CRP — was highest [7]. This finding is important less because it is surprising and more because it comes from a rigorously monitored randomized trial population with centrally scored radiographs, which reduces some of the confounding that affects observational cohorts.

A later analysis directly built on this question, examining radiographic progression according to baseline CRP levels and other risk factors in PsA patients treated with either tofacitinib or adalimumab; the study reported that higher baseline CRP was associated with greater structural progression risk across both treatment arms, reinforcing CRP's role as a treatment-independent prognostic marker rather than one specific to a single drug class [8]. That treatment-arm-independence is a meaningful piece of evidence: it suggests CRP's predictive signal reflects something about the patient's underlying inflammatory trajectory rather than an artifact of how a particular therapy modulates the marker.

More recently, a study examining the role of clinical and biochemical inflammation in structural progression directly compared composite indices incorporating CRP (such as the Disease Activity Index for Psoriatic Arthritis and 28-joint Disease Activity Score with CRP) against purely clinical measures, reporting that biochemical inflammation captured by CRP-inclusive composite scores contributed meaningfully to explaining subsequent structural damage, though clinical joint counts and composite disease activity retained substantial independent predictive value as well — indicating that CRP is a genuine but partial contributor to structural risk prediction rather than a sufficient one on its own [9].

These three studies, spanning different treatment eras and different composite score frameworks, converge on a consistent qualitative conclusion: elevated CRP is associated with a higher risk of subsequent radiographic progression in PsA, but it explains only part of the variance, and its predictive value appears to be additive to, rather than a replacement for, clinical joint assessment.

Earlier Foundational Work

This is not an entirely new line of inquiry. Multivariate

relative-risk modeling of clinical indicators of progression in PsA, going back three decades, already identified the number of actively inflamed joints and, notably, particular HLA antigen associations as indicators of a more destructive disease course, establishing early that joint-level inflammatory burden — not merely the presence of psoriasis or arthritis per se — tracked with structural risk [10]. Around the same period, prospective early-arthritis clinic cohorts following patients from their first synovitis episode documented that a substantial proportion of PsA patients already showed radiographic damage within the first two years of symptom onset, often before treatment escalation, underscoring how early in the disease course the inflammation-to-damage window can close [11]. Together, this earlier body of work established the conceptual foundation — active joint inflammation predicts subsequent damage — that the CRP-focused studies above have since tried to operationalize with a single, easily measured circulating marker.

Interpreting Convergent Findings Across Different Trial Populations

It is worth pausing on why the convergence across the ADEPT subanalysis, the tofacitinib/adalimumab comparison, and the clinical-versus-biochemical inflammation study is more persuasive than any one study alone [7,8,9]. These three analyses differ in treatment exposure (a TNF inhibitor alone, a Janus kinase inhibitor compared against a TNF inhibitor, and a mixed-treatment observational cohort), in the composite disease activity frameworks used, and in the statistical approach to adjusting for baseline confounders such as joint count and prior damage. A marker that shows an association with progression under only one of these conditions would be a fragile finding, plausibly explained by unmeasured confounding specific to that dataset or that drug's mechanism of action. A marker that shows a directionally consistent association across all three — different drugs, different eras, different analytic approaches — is doing something closer to what a genuinely useful prognostic marker should do: tracking an underlying biological risk that persists regardless of which downstream therapeutic lever is being pulled. That said, "directionally consistent" is a weaker claim than "quantitatively precise," and none of these studies alone, nor the three in aggregate, provide the kind of externally validated risk-prediction model (with

reported calibration and discrimination statistics in an independent cohort) that would be needed to use baseline CRP as a formal, individual-patient risk score in clinical practice.

5. Beyond CRP: Soluble Biomarkers and Composite Panels

Because CRP and ESR are non-specific acute-phase reactants shared across essentially all inflammatory diseases, a parallel research program has sought PsA-specific soluble biomarkers, both to improve diagnostic discrimination from psoriasis-without-arthritis and, more relevantly here, to see whether panels of markers outperform CRP alone as prognostic tools.

Table 1: Inflammatory markers and imaging modalities examined in the literature synthesized in this article as candidate predictors of joint damage or disease transition in psoriatic arthritis, with the principal finding reported by each cited source. [7,8,9,12,13,14,16,6,18,17].			
Marker / Modality	Study	Context	Principal Reported Finding
Baseline CRP	Gladman et al. [7]	RCT subanalysis	Independent predictor of radiographic progression; greatest treatment benefit in high-CRP patients
Baseline CRP	van der Heijde et al. [8]	RCT, two drug classes	Higher baseline CRP associated with greater progression risk across both treatment arms
Composite indices (CRP)	Borst et al. [9]	Observational cohort	Biochemical inflammation contributes to, but does not replace, clinical measures in predicting structural progression
Soluble biomarker panel	Chandran et al. [12]	Case-control	Panel differentiates PsA from psoriasis with better discrimination than CRP alone
Novel serum biomarker panel	Cretu et al. [13]	Case-control	Refined panel improves discrimination over standard clinical/laboratory measures
CXCL10	Abji et al. [14]	Prospective cohort	Candidate biomarker for identifying psoriasis patients who later develop PsA
CRP and bone markers	Wagner et al. [16]	Golimumab cohort	CRP and bone-resorption markers fall with clinical improvement under anti-TNF therapy
MSK ultrasound findings	Naredo et al. [6]	Case-control	High prevalence of subclinical inflammation undetected by exam or serum markers

Marker / Modality	Study	Context	Principal Reported Finding
MRI osteitis and synovitis	Poggenborg et al. [18]	GRAPPA consensus report	MRI lesions correlate with subsequent site-specific structural damage; scoring still maturing
Radiographic progression, IL-12/23 blockade	Kavanaugh et al. [17]	RCT (ustekinumab)	Cytokine-pathway-targeted therapy inhibits radiographic progression vs. placebo

Work from the University of Toronto psoriatic disease program found that a panel of soluble biomarkers — including markers of matrix turnover, angiogenesis, and cytokine signaling — could differentiate PsA patients from patients with psoriasis but no arthritis with better discrimination than clinical variables or CRP alone, suggesting that some biological signal relevant to joint involvement is present in serum but not well captured by conventional acute-phase testing [12]. A follow-up study from the same group tested a refined panel of novel serum biomarkers for the same differentiating task and again found improved discrimination over standard clinical and laboratory measures, reinforcing that composite biomarker panels carry additional information beyond CRP, at least for distinguishing PsA from psoriasis alone [13].

Chemokine-based markers have also been explored specifically as predictors of disease transition. CXCL10, an interferon-inducible chemokine involved in T-cell trafficking, was reported as a possible biomarker for identifying which psoriasis patients were more likely to go on to develop psoriatic arthritis, based on a cohort of psoriasis patients followed longitudinally, some of whom transitioned to PsA during observation [14]. While this evidence speaks primarily to disease transition (psoriasis to PsA) rather than joint damage progression within established PsA, it is relevant to this synthesis because it illustrates the same underlying logic — that circulating markers of a specific inflammatory pathway can carry prognostic information that generic acute-phase reactants miss — applied one step earlier in the disease trajectory.

A systematic literature review of biomarkers in PsA, surveying this broader landscape, concluded that while numerous candidate soluble markers (including matrix metalloproteinases, cytokines, and bone turnover markers) have shown associations with disease activity or structural outcomes in individual studies, few have been validated across independent cohorts with the

rigor needed for clinical adoption as prognostic tools, and CRP — despite its limitations — remains the most consistently validated and widely available marker in this space [15]. This review's conclusion is a useful corrective to any temptation to treat novel biomarker findings as more clinically mature than they are: promising signal in single cohorts is common, cross-validated clinical utility is rare.

Inflammatory Markers Under Biologic Therapy

A related body of evidence examines how inflammatory and bone-remodeling markers behave during treatment, which indirectly speaks to their prognostic relevance. In a study of PsA patients treated with the TNF inhibitor golimumab, improvement in clinical response measures was accompanied by significant reductions in CRP alongside markers of bone resorption and, to a lesser extent, changes in markers of bone formation, suggesting that the inflammatory and bone-remodeling axes move together under effective anti-inflammatory treatment [16]. This kind of treatment-response biomarker data does not, on its own, establish that baseline CRP predicts progression, but it does support the underlying causal story — that suppressing the inflammatory signal captured by CRP plausibly slows the downstream bone-remodeling processes that produce structural damage — which is the mechanistic premise the prognostic studies above are implicitly testing.

Radiographic outcome data from biologic trials targeting different cytokine pathways add a further layer. An integrated analysis of radiographic data from the PSUMMIT-1 and PSUMMIT-2 trials of ustekinumab, an anti-IL-12/23 p40 monoclonal antibody, found that ustekinumab treatment inhibited radiographic progression relative to placebo in patients with active PsA, consistent with a causal link between the IL-23 pathway (upstream of much of the inflammatory and bone-remodeling activity discussed above) and structural outcomes [17]. That a drug targeting a specific cytokine axis measurably alters radiographic trajectories reinforces, again indirectly, that the inflammatory processes reflected in serum markers are not epiphenomenal bystanders but plausible drivers of the damage being predicted.

The Diagnostic-Versus-Prognostic Distinction

A methodological point deserves emphasis when reading the soluble-biomarker literature: most of these studies, including the two Toronto-group panels

discussed above, were designed and validated as diagnostic tools — distinguishing PsA from psoriasis without arthritis — rather than as prognostic tools predicting the rate or extent of subsequent joint damage within a population already known to have PsA [12,13]. A biomarker can be an excellent diagnostic discriminator (separating "has PsA" from "does not have PsA") while carrying little or no prognostic information (predicting "how much structural damage this PsA patient will accrue"), because these are different statistical tasks with different optimal marker properties. The CXCL10 findings sit somewhat between these two tasks, since they were derived from a cohort observed prospectively as patients transitioned from psoriasis to PsA, making them closer to prognostic evidence for disease onset, though still distinct from prognostic evidence for structural progression after PsA is established [14]. This distinction is not a criticism of the underlying studies, which were appropriately designed for their stated purpose, but it is a reason for caution before assuming that a marker validated for diagnosis will automatically transfer to structural-risk prediction — a transfer that, per the systematic review discussed below, has rarely been directly tested [15].

6. Imaging as a Window into Subclinical Inflammation

One of the more consistent findings in the PsA imaging literature is that clinical examination and even CRP substantially underestimate the true burden of synovial and enthesal inflammation. A prospective case-control study using musculoskeletal ultrasound found a high prevalence of subclinical synovitis and enthesopathy in patients with psoriasis but no clinically apparent arthritis, detecting inflammatory changes on ultrasound in a substantial proportion of patients who had entirely normal joint examinations and, in many cases, normal inflammatory markers [6]. This finding has an important implication for the present topic: if serum CRP frequently fails to flag inflammation that is nonetheless present and detectable by imaging, then CRP-based prognostic models will systematically misclassify a subset of patients as "low inflammatory burden" who, by an imaging-based definition, are not.

Magnetic resonance imaging has been proposed as a complementary or even superior tool for this purpose, given its sensitivity to synovitis, osteitis (bone marrow edema), tenosynovitis, and enthesitis simultaneously. A

GRAPPA-sponsored report on the state of MRI in PsA summarized emerging consensus that MRI-detected inflammatory lesions, particularly osteitis, correlate with subsequent structural damage at the same anatomic site more directly than global disease activity measures, and that MRI scoring systems for PsA were, at the time, still being refined and validated for use as outcome measures in clinical trials and, prospectively, as prognostic tools in individual patients [18]. The GRAPPA report's cautious framing — that MRI shows promise but standardized, validated scoring was still a work in progress — is a useful marker of how much of the imaging-biomarker literature in this space remains at the stage of demonstrating feasibility and correlation rather than delivering a clinically deployable prognostic instrument.

Taken alongside the early synovitis clinic findings discussed earlier, in which a meaningful fraction of PsA patients already had radiographic damage within two years of symptom onset [11], the imaging literature suggests that the inflammatory processes driving structural progression are frequently active and detectable well before they manifest as elevated serum markers or clinically swollen joints — a mismatch that has real implications for how aggressively "quiet" patients should be monitored.

The Subclinical Inflammation Problem in Practice

The clinical implication of the ultrasound and MRI findings is not merely academic. If a substantial fraction of patients with psoriasis, and by extension a substantial fraction of PsA patients in apparent clinical remission, harbor active but subclinical synovitis or enthesitis, then any structural-risk model built solely on CRP and joint examination is working from an incomplete picture of the true inflammatory state driving progression [6]. This has practical consequences for how "low risk" is defined at the bedside: a patient with a normal CRP, no swollen joints, and no enthesal tenderness on examination might still be accumulating imaging-detectable inflammation with structural consequences, a scenario the imaging literature suggests is not rare. Whether routine imaging surveillance in clinically quiescent patients is a cost-effective or even feasible strategy at scale is a separate question from whether such inflammation exists and predicts damage — the existing literature speaks much more clearly to the latter than the former, and pragmatic imaging use in most clinical settings remains targeted (evaluating a specific

symptomatic joint or enthesal site) rather than used as a periodic screening tool across all domains in asymptomatic patients.

7. Inflammatory Markers in the Context of Treat-to-Target and Clinical Guidelines

The clinical relevance of inflammatory-marker-based prediction is best understood against the backdrop of treat-to-target strategy in PsA, which has become the dominant paradigm for guiding therapy escalation. GRAPPA treatment recommendations incorporate composite measures of disease activity across the multiple domains of PsA, and while these recommendations do not treat CRP as a standalone treatment trigger, they situate acute-phase reactants as one input among several — alongside joint counts, enthesitis and dactylitis indices, and patient-reported outcomes — in composite activity measures used to guide escalation decisions [19]. This reflects the same conclusion drawn from the direct progression studies above: CRP contributes to, but does not substitute for, a broader clinical assessment.

Minimal disease activity (MDA), a widely used treatment target in PsA, is itself defined by a set of criteria that includes tender and swollen joint counts, patient pain and global assessments, and Psoriasis Area and Severity Index, but notably does not require a specific CRP threshold, reflecting a deliberate design choice to avoid over-weighting a marker with known limitations in this disease [20]. A cohort study examining predictors of sustained MDA found that patients achieving and maintaining this target had, on average, lower baseline disease activity across multiple domains, including inflammatory burden, but that achieving MDA at any single time point did not guarantee its maintenance, with a meaningful proportion of patients relapsing over longer follow-up — a reminder that a single favorable inflammatory-marker snapshot is a poor substitute for longitudinal monitoring [20].

8. Open Challenges and Future Directions

Several gaps remain evident from this literature. First, most of the direct evidence linking CRP to radiographic progression comes from randomized trial subanalyses and observational cohorts in patients with established, often longer-duration PsA; there is comparatively less direct longitudinal evidence in early or very early disease, precisely the window in which prognostic

information would be most clinically actionable and in which imaging studies suggest inflammation is already active but serum markers may not yet reflect it [11,6]. Second, no soluble biomarker panel reviewed here has achieved the kind of cross-cohort, prospectively validated status that would support routine clinical deployment as a structural-progression risk score; the systematic review of PsA biomarkers is explicit on this point, noting that promising single-cohort associations vastly outnumber validated, reproducible findings [15]. Third, the dual erosive/osteoproliferative biology of PsA means that a single "inflammation score," however constructed, may be poorly suited to predicting the balance between bone loss and new bone formation in a given joint, since these processes may respond differently to the same upstream inflammatory signal [4]. Fourth, imaging-based biomarkers, while sensitive, remain resource- and expertise-intensive relative to a blood draw, and standardized, validated scoring systems for prognostic (as opposed to purely descriptive) use are still maturing, particularly for MRI [18].

A further challenge is the practical one of how a treat-to-target framework should incorporate imperfect prognostic markers without either ignoring them or over-relying on a single number. The GRAPPA recommendations' approach — folding CRP into composite, multi-domain activity measures rather than using it as an isolated trigger — is a reasonable pragmatic compromise given current evidence, but it is not the same as a validated structural-risk prediction tool, and the field still lacks a well-validated multivariable model that integrates CRP, imaging findings, and clinical risk factors into a single, clinically usable structural-progression risk estimate for individual patients [19,9].

9. Conclusion

The literature reviewed here supports a consistent but modest conclusion: elevated CRP, and to a lesser extent ESR, are real, reproducible, treatment-arm-independent predictors of subsequent radiographic joint damage progression in psoriatic arthritis, evident across randomized trial subanalyses and observational cohorts spanning different eras of PsA therapy [7,8,9]. They are not, however, sufficient predictors on their own. Soluble biomarker panels and chemokines such as CXCL10 add discriminative information, particularly for distinguishing PsA from psoriasis alone, but remain

short of validated prognostic tools for joint damage progression specifically [12,13,14,15]. Imaging modalities, especially musculoskeletal ultrasound and MRI, reveal a substantial reservoir of subclinical synovial and enthesal inflammation that serum markers routinely miss, suggesting that the true inflammatory burden driving structural damage in a meaningful subset of patients is simply invisible to a CRP assay [6,18]. Foundational cohort work going back three decades already established that joint-level inflammatory burden predicts a more destructive disease course, a finding the more recent, marker-specific literature has largely reaffirmed and refined rather than overturned [10,11]. For now, the most defensible clinical use of inflammatory markers in PsA is as one input among several in a multidomain assessment — exactly the role current treatment guidelines already assign them — rather than as a standalone prognostic test, with the integration of imaging-based subclinical inflammation data into validated, individual-level structural-risk models remaining an open and clinically important research priority [19,2].

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Conflict of Interest

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Data Availability Statement

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Ethical Approval

Not applicable. This article involved no human participants, animal subjects, or collection of primary clinical data, and required no ethical committee review.

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