

The diagnosis and treatment of early psoriatic arthritis

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Abstract | Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disorder associated with a heterogeneous disease presentation, varied disease expression and an unpredictable but often chronically destructive clinical course. Joint damage can occur early in the disease; indeed, several imaging modalities have demonstrated subclinical joint involvement in psoriasis patients without musculoskeletal signs or symptoms. Efforts are underway to validate questionnaires that will enable dermatologists to screen patients with psoriasis for the presence of musculoskeletal disease. To date, the use of therapies in patients with early PsA has not been reported in randomized controlled trials. Moreover, conventional agents are partially effective in established PsA but, in general, trials with DMARDs have not included validated outcome measures for the different manifestations of PsA. Tumor necrosis factor antagonists can alleviate the signs and symptoms of established psoriatic arthritis and inhibit radiographic progression, but the therapeutic impact of early intervention with these agents requires further study. The extent of disease and the presence of comorbidities should be used to guide treatment decisions and to minimize adverse events.

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Learning objectives

Upon completion of this activity, participants should be able to:

- 1 Describe the patterns of onset of psoriatic arthritis (PsA) in patients with psoriasis.
- 2 Describe the questionnaires that are available for identifying progression from psoriasis to PsA.
- 3 Identify the most useful imaging studies for early detection of PsA.
- 4 Describe the role of the Classification criteria for Psoriatic Arthritis (CASPAR).
- 5 Identify options in the treatment of early PsA.

Competing interests

The authors, the Journal Editor J. Buckland and the CME questions author D. Lie declare no competing interests.

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disorder notable for its diversity in presentation, expression and clinical course. Disease presentation can vary from subtle enthesal pain to arthritis mutilans, a highly destructive form of arthritis. The expression of clinical features is also quite varied and can involve a wide array of tissues, including synovium, cartilage, bone, entheses and tendons, in addition to skin and nails. Not surprisingly, the clinical course of PsA is unpredictable, although evidence indicates that it can be a debilitating condition that leads to increased morbidity and mortality.¹ Radiographic damage can occur within 2 years of disease onset in almost half of patients with PsA, and the disease follows a chronic, progressive course in most patients.^{2,3} The recognition that PsA can lead to marked joint destruction with consequent impairment to quality of life has modified the treatment paradigm. Increased emphasis is now placed on inhibition of joint damage, in addition to reducing pain and improving function. These goals can best be achieved by early diagnosis and intervention.

One of the most intriguing features of PsA is that it usually arises in patients with pre-existing psoriasis. Indeed, in about 70% of PsA cases the onset of psoriasis precedes that of arthritis, whereas the arthritis precedes the skin disease in only about 15% of cases, and the two occur simultaneously in the other 15%.¹ Thus, investigators and clinicians have a unique opportunity to screen a defined population with a distinctive cutaneous phenotype in order to identify patients with PsA early in disease course. In this Review, we discuss

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diagnostic strategies to identify patients with early psoriatic musculoskeletal inflammation and examine current treatment strategies, with an emphasis on critical variables that clinicians should consider when they ponder therapeutic options for patients with PsA of recent onset.

Defining 'early' PsA

The term 'early PsA' remains imprecisely defined, and the duration of 'early' disease can range from several months to anything less than 5 years.^{2,4-6} The development of a universally accepted definition of early PsA has been confounded by multiple factors. PsA can present with a wide spectrum of clinical manifestations, as described above, which can delay diagnosis. Furthermore, the absence of disease-specific biomarkers, such as anti-cyclic citrullinated peptide antibodies in the case of rheumatoid arthritis (RA), leads to reliance on clinical phenotype, which may come to medical attention at a more advanced disease stage. Also, joint inflammation could be clinically underestimated and may not be detected until damage is noted on radiographs or physical examination. Patients with PsA are reported to have less joint tenderness than patients with RA.⁷ Moreover, axial inflammation may be clinically silent.⁸ Additionally, until 2006, validated classification criteria for PsA were not available; therefore, it was difficult to know if patients in clinical trials truly had PsA. It is interesting to note that PsA accounts for only 5–13% of inflammatory joint disease in Early Arthritis Clinics. That this rather low figure reflects diagnostic challenges associated with this disorder, particularly in the initial stages, is highly likely.^{2,4}

Early joint manifestations in psoriasis

The role of questionnaires

In the majority of patients with PsA, the onset of psoriasis precedes the arrival of joint symptoms by approximately 10 years;^{1,9} furthermore, undiagnosed PsA is highly prevalent in patients with psoriasis.^{10,11} The delay in the emergence of arthritis after the initial presentation of psoriasis provides a unique opportunity to screen patients followed in dermatology clinics for early evidence of joint disease. A brief interview that includes a few key questions regarding joint symptoms, morning stiffness and function could help uncover evidence of PsA and prompt a subsequent referral to a rheumatologist. Time constraints on many dermatologists, however, might preclude routine questioning regarding joint symptoms. With this in mind, several screening tools, to be completed by the patient in the dermatologist's waiting room or at home, have been designed to identify those psoriasis patients with symptoms of inflammatory arthritis (Table 1).¹²

On the Psoriasis and Arthritis Questionnaire (PAQ), a score of 7 or higher (out of a possible score of 10) predicts PsA in patients with psoriasis with a sensitivity of 85% and a specificity of 88%.¹³ A validation study of the above questionnaire by Alenius *et al.*¹⁴ reported a

Key points

- Psoriatic arthritis (PsA) follows a chronic, progressive course in the majority of patients, and joint damage occurs early in the disease course
- Clinical trial data for the treatment of early PsA are not yet available, in sharp contrast to the high-level evidence published for therapy in early rheumatoid arthritis
- Ultrasonography and MRI can identify subclinical joint disease in patients with psoriasis and can assist in the early diagnosis and assessment of joint damage in patients with PsA
- Early treatment of PsA will probably suppress inflammation and alter the disease course, but evidence to support this statement is not yet forthcoming
- The potential advantages of early therapy further underscore the need for early diagnosis but point to the need for prognostic markers that will help refine treatment stratification
- Trials to demonstrate the efficacy of targeted biologic therapies and DMARDs for early PsA will test the validity of early intervention as a strategy to alter the disease course

Table 1 | Questionnaires for screening patients with psoriasis for arthritis

Questionnaire feature	ToPAS ¹⁶	PASE ¹⁵	PAQ ¹³
Number of questions	12	15	12
Population to be screened	General	Patients with psoriasis	Patients with psoriasis
Sensitivity	94%	82%	85%
Specificity	92%	73%	88%
Positive predictive value	82%	NA	NA
Negative predictive value	98%	NA	NA
Detects presence of disease activity?	No	Yes	Yes

Abbreviations: NA, not available; PAQ, Psoriasis and Arthritis Questionnaire; PASE, Psoriatic Arthritis Screening and Evaluation; ToPAS, Toronto Psoriatic Arthritis Screening questionnaire.

sensitivity of 60% and specificity of 62% for prediction of arthritis and/or enthesitis. A modification of the PAQ did increase the sensitivity and specificity to 68.7% and 77.8%, respectively, with a positive predictive value of 60.5%, but the authors concluded that the low sensitivity and predictive value of this set of questions limits its value for detecting arthritis in patients with psoriasis.

The Psoriatic Arthritis Screening and Evaluation (PASE) questionnaire, also developed for use by dermatologists, has shown promise as an effective screening tool for identifying patients with PsA.¹⁵ The PASE consists of questions that assess symptoms (7 questions; maximum score 35) and function (8 questions; maximum score 40) and gives an overall score calculated by summing the responses to all questions. The Toronto PsA screening questionnaire (ToPAS) was designed by Gladman *et al.*¹⁶ by means of a review of the clinical features of patients with PsA. The ToPAS comprises 12 questions selected on the basis of the expert opinion of rheumatologists and dermatologists. The inclusion of pictures of skin and nail lesions distinguishes it from the other screening questionnaires. It was developed to screen for PsA regardless of whether a patient has psoriasis, and proved

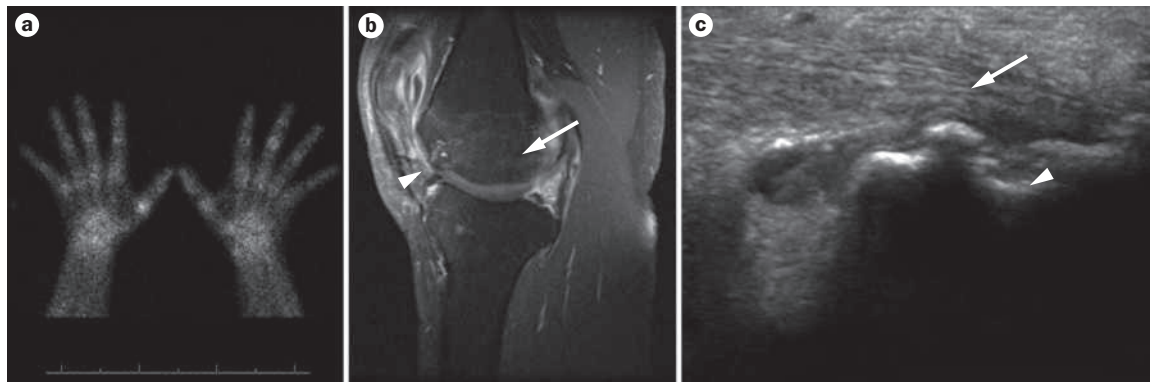


Figure 1 | Imaging studies in early psoriatic arthritis. **a** | Nuclear bone scan showing increased uptake of technetium in the small joints of the hands and carpus, which suggests the presence of articular inflammation, in a patient with psoriasis referred to a rheumatology clinic for back pain. **b** | MRI of a patient with early psoriatic arthritis (disease duration of 12 months) showing extensive bone marrow edema (arrow) and soft tissue inflammation (arrowhead). **c** | Ultrasound image of Achilles tendinopathy in a patient with early psoriatic arthritis (joint symptoms duration of 2 months) showing thickening of the Achilles tendon (arrow) and erosions at the enthesitis (arrowhead). Printed with permission from R. Thiele.

to be highly sensitive and specific in identifying patients with PsA in various clinical settings.

A well-designed screening instrument should both detect and help determine the prevalence of PsA. A screening tool for use in clinical practice should be brief, easy to administer and be highly sensitive, whereas a screening tool for use in research should have a high specificity for PsA.¹² To date, however, no consensus exists on the most appropriate screening method for use in either setting.¹² One approach to developing the optimum tool may be to combine the best elements of each questionnaire. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) are validating the questionnaires discussed above in various patient populations.

The role of imaging studies

Over the past 30 years, investigators have turned to a variety of imaging modalities to study the joints and periarticular structures in psoriasis patients without musculoskeletal complaints or signs of inflammation. Bone scintigraphy, for instance, reveals the extent of joint inflammation at various sites and, despite its low specificity and poor resolution, may be more sensitive than clinical examination or radiography in the detection of early joint involvement in psoriasis (Figure 1a).¹⁷ A Canadian study compared periarticular uptake of technetium diphosphonate (TcDP) in 12 patients with active psoriasis and 12 patients with other skin diseases,¹⁸ all of whom had skin disease of less than 5 years' duration and were free of symptoms or signs of joint disease. Generalized uptake of TcDP was higher in the psoriasis patients compared with the control group, which reflected a greater extent of joint involvement in the former group. The uptake of TcDP was decreased after 2 weeks' therapy with coal tar and ultraviolet light, which suggests a link between the activity of skin disease

and uptake of TcDP. These findings were replicated in a study from Pakistan, in which 50 patients with extensive plaque psoriasis but no joint disease were compared with 25 controls.¹⁹ Bone scans were positive in 35 of the psoriasis patients but only 4 of the controls ($P < 0.001$). The results of this study further support the concept that bone scintigraphy could be useful for detecting subclinical joint disease in patients with psoriasis.

MRI could also be more sensitive than both clinical examination and radiography in detecting inflammatory joint disease.²⁰ In addition, MRI enables the visualization of early features of inflammatory disease, such as synovitis, enthesitis, osteitis and bone erosions (Figure 1b).²¹ Offidani *et al.*²² evaluated the frequency of hand involvement in patients with psoriasis free of joint symptoms using both MRI and plain radiography. Imaging studies of 25 consecutive patients with psoriasis, with disease duration that ranged from 1 month to 10 years, were compared with those of 12 healthy individuals. Except for one joint cyst, no abnormalities were noted on radiographs or MRI scans of the control individuals. By contrast, one or more signs of arthritis were found in 68% of MRI images and 32% of radiographs of patients with psoriasis. MRI detected bone erosions in 28% of psoriasis patients while radiography revealed erosions in 20%. Interestingly, 46% of psoriasis patients had bone marrow edema in the small joints and carpal bones. In this study, no correlation was observed between the degree of skin involvement and MRI findings. Another MRI study performed on the feet of 26 patients with psoriasis with no evident musculoskeletal symptoms or signs also reported frequent abnormalities in the psoriasis group (24 [92%] of 26 patients), whereas none were found in the 10 healthy controls. The MRI abnormalities included tendinitis, bone marrow edema, bone erosions, enthesopathy, bursitis and other bone and soft tissue abnormalities.²³

Musculoskeletal ultrasonography has several characteristics that are advantageous for the diagnosis of subclinical joint involvement in patients with psoriasis. This office-based procedure is relatively inexpensive and, most importantly, provides visualization of entheses, tendons, synovium, cartilage, and bone and tissue vascularity.²⁴ A case-control study from Italy used ultrasound examinations to evaluate enthesitis in 30 patients with chronic plaque psoriasis and no clinical manifestations of joint or enthesal disease and 30 controls matched for age and sex.²⁵ Of note, patients with psoriasis had received no systemic therapy for at least 3 months before ultrasonography and clinical examination. Ultrasonography of the entheses revealed significantly more abnormalities in patients with psoriasis than in controls. Similar findings have been reported in other trials of patients with psoriasis and of asymptomatic PsA patients.^{26–29} The results of these studies support the use of tendon ultrasonography in the early detection of PsA. Moreover, the findings of enthesal imaging abnormalities in asymptomatic psoriasis patients dovetails with the recent work of McGonagle and others³⁰ who have put forth the concept that enthesitis is one of the first steps in the development of PsA.

The role of classification criteria

The lack of a validated case definition for PsA has been a major impediment to scientific research in this disease. Several classification criteria have been proposed over the years, but none have been validated or agreed upon.³¹ In 2006, an international group of rheumatologists proposed the Classification of Psoriatic Arthritis (CASPAR) criteria, based on the results of a large prospective study (Box 1).³² The CASPAR criteria were developed to be used in the context of clinical research and had a sensitivity and specificity of 91.4% and 98.7%, respectively, in patients with PsA when compared with patients with other forms of inflammatory arthritis (primarily RA). A major limitation of this study was, however, that the patients enrolled had longstanding disease (mean disease duration 12.5 years). Another challenge is that these criteria require patients to have inflammatory arthritis, a finding that is open to interpretation and, as discussed above, is not always evident, particularly in the early stages of PsA.

The high sensitivity and specificity of the CASPAR classification criteria suggest that they might also be used as diagnostic criteria for PsA. Several studies have tested the sensitivity of the CASPAR criteria for detecting early PsA.^{33,34} In a retrospective study of 107 patients with early PsA (disease duration of less than 2.5 years) seen at a specialist PsA clinic over a 14-year period, 106 of the patients satisfied the CASPAR criteria (99.1% sensitivity).³³ A subsequent prospective study of patients with a mean disease duration 15.8 weeks, however, noted a sensitivity of only 77.3%.³⁴ Generally, classification criteria should not be used for diagnostic purposes; however, the role of CASPAR criteria in the

Box 1 | CASPAR classification criteria³²

Patients fulfill the CASPAR (Classification criteria for Psoriatic Arthritis) criteria if they have inflammatory joint disease (peripheral, axial or enthesal involvement) and a score of three or more points from the five categories below.

1. Evidence of current psoriasis, a personal history of psoriasis, or a family history of psoriasis

- Current skin or scalp disease as diagnosed by the health care provider on physical examination (2 points)
- History of psoriasis reported by the patient or a health care provider (1 point)
- Family history of psoriasis in a first-degree or second-degree relative (1 point)

2. Nail involvement

- Features of psoriatic nail dystrophy apparent on physical examination, including onycholysis, pitting and hyperkeratosis (1 point)

3. Negative test result for the presence of rheumatoid factor

- Negative results of test for rheumatoid factor, preferably performed by any method except latex assay but preferably by enzyme-linked immunosorbent assay or nephelometry (1 point)

4. Either current dactylitis or a history of dactylitis

- Current dactylitis as diagnosed by the health care provider on physical examination (1 point)
- History of dactylitis as recorded by a health care provider (1 point)

5. Radiographic evidence of new bone formation

- Appearance of juxta-articular new bone formation on radiographs of the patient's hands or feet (1 point)

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identification of patients with early PsA remains to be established.

Evaluating early PsA with imaging studies

Imaging modalities can detect subclinical joint inflammation, as outlined above, and can also assist the clinician in the evaluation of early PsA. Scarpa *et al.*³⁵ used bone scintigraphy and ultrasonography to delineate joint and enthesal disease in 47 consecutive patients referred to an early PsA clinic. 29 patients had PsA (on the basis of the Moll and Wright criteria³⁶) while the other 18 were classified as having PsA in the absence of psoriatic skin disease. Full clinical assessments and bone scintigraphy were performed in all patients, in addition to plain radiography of clinically involved joints. The median number of joints and/or entheses with increased tracer uptake on bone scintigraphy was significantly greater than the median number of affected joints and/or entheses detected by the clinical examination ($P < 0.001$). Ultrasonography revealed synovial effusion and signs of synovitis in all 186 joints in which tracer uptake was increased, but in only 2 of the 94 control sites assessed. The marked discrepancy between the results of clinical and imaging examination further supports the notion

that joint involvement in early PsA may be clinically underestimated. Furthermore, it supports the theory that early PsA is an entheso-articular syndrome.³⁰

Marzo-Ortega *et al.*³⁷ compared MRI findings in 10 patients with early PsA and 10 patients with early RA, in each case defined as disease duration of less than 2 years. MRI (1.5 Tesla) of the swollen hand (identified by clinical examination) revealed that synovitis and tenosynovitis were significantly more common in patients with RA than in those with PsA. No difference was noted in the number or size of erosions between the two groups. The degree of bone edema was comparable in both groups, although the distribution of edema was more diffuse in the PsA group. Inflammatory changes were localized to the synovium in the RA patients; by contrast, extracapsular involvement was observed in the patients with PsA, as has also been described in other studies.^{38,39}

Taken together, these studies demonstrate that patients with early-onset PsA manifest a wide range of findings on imaging studies. Scintigraphy can reveal articular inflammation, and musculoskeletal ultrasonography and MRI enable visualization of enthesitis, synovitis and erosions (Figure 1c). Additionally, the descriptions of the enthesal abnormalities might help gain further insights into the pathogenesis of PsA.

Treatment of early PsA

Treatment decisions can be difficult in PsA owing to the wide diversity and various combinations of clinical manifestations that can occur in a single patient. Furthermore, different structures, including joints, skin, entheses, nails and other soft tissues, may be involved at varying degrees of severity. Until about 10 years ago, treatment of PsA was extrapolated from studies in RA, with outcome measures centered on peripheral arthritis and, to a lesser extent, skin disease. It is now appreciated that enthesitis, dactylitis and axial disease can also limit function and erode quality of life, so these outcome measures are now included in clinical trials. Moreover, a meta-analysis of DMARD therapies for PsA noted well-founded evidence for efficacy only with sulfasalazine and parenteral, high-dose methotrexate, which thereby highlighted the difference in response to treatment between patients with RA and PsA.⁴⁰ Interestingly, this study also found uniform improvements in the placebo arms of the PsA trials, a finding that has important implications in that it argues against the use of uncontrolled data in treatment decisions for PsA.⁴⁰

DMARDs and NSAIDs

Data regarding the efficacy of therapeutic agents in early PsA are not yet available, but in 2008 GRAPPA published evidence-based recommendations for treating established PsA.⁴¹ Most patients are initially treated with NSAIDs.⁴² This approach is not without the risk of potentially severe adverse effects, particularly given evidence that the prevalence of myocardial infarction is sixfold higher in young patients with severe psoriasis

compared with age-matched patients without psoriasis.⁴³ Another concern is that NSAIDs can trigger the onset of psoriasis in some patients.⁴⁴ Although available data support the use of DMARDs in the treatment of peripheral joint disease in PsA, the effect size in these studies was quite modest and, in the case of leflunomide, adverse effects can be a problem.⁴² Moreover, the trials involving DMARDs did not include a systematic analysis of radiographic end points. Methotrexate remains the most commonly prescribed DMARD for PsA, although high-level evidence supporting the use of this agent has not been generated from controlled trials.⁴⁵ Furthermore, the ability of this agent to suppress articular or periarticular inflammation in early disease, as detected by clinical examination or imaging, has not been evaluated. Liver toxicity remains the primary concern in patients taking methotrexate and, given the high prevalence of obesity and concomitant diabetes and metabolic syndrome in patients with psoriasis, the risk of liver damage may be higher in this group than in patients with RA.⁴⁶

Early arthritis clinics have helped examine the efficacy of DMARD therapy in PsA in observational studies. In 2008 the Swedish Early PsA Registry reported data on 135 patients with PsA of less than 2 years' duration, based on the CASPAR criteria, who were followed over 2 years.⁴⁷ Early PsA was defined as inflammatory joint symptoms and signs compatible with PsA of less than 24 months duration. Although approximately 50% were receiving DMARD therapy, some of the DMARD-treated patients without radiographic damage at initial presentation developed radiographic damage at 2 years. No difference in radiological outcome or number of patients to achieve remission was noted between patients who received therapy and those not treated with DMARDs. Kane *et al.*² reported data from a cohort of 129 patients with PsA (mean disease duration 9.9 months) who were followed at their early arthritis clinic over a period of 2 years. Only 12% were on DMARDs at initial presentation. This proportion increased to 59% at 1 year, and was 56% at 2 years. Sulfasalazine and methotrexate were the most commonly prescribed DMARDs. Remission, defined as the absence of fatigue, morning stiffness of <15 min, no joint pain, complete absence of joint tenderness or swelling on examination and an erythrocyte sedimentation rate <20 mm/h, was noted in 26% of patients at 1 year and 21% at 2 years. Follow-up radiographic findings were present in 86% of all patients, and revealed increases in erosions, joint space narrowing and/or periostitis at 2 years. In addition to showing that significant functional impairment and radiographic damage occur early in the disease course, this study highlights that, despite significant improvement in clinical outcomes with DMARD therapy, progressive joint damage can occur in the first 24 months of onset of PsA.

Tumor necrosis factor inhibitors

The arrival of tumor necrosis factor (TNF) antagonists has profoundly altered the therapeutic landscape for

psoriasis and PsA. To date, four anti-TNF agents—etanercept, infliximab, adalimumab and golimumab—have been approved for the treatment of PsA by the US FDA.^{48–51} In addition to improving outcomes of skin and joint disease, these agents also significantly improve quality of life and function and markedly inhibit radiographic progression in patients with PsA. It should be noted, however, that these benefits were noted in patients with established disease—in phase III trials, the mean disease duration was >7.6 years.^{48–51}

Despite the lack of data from clinical trials regarding the efficacy of anti-TNF therapies in early PsA, three lines of evidence suggest that these agents will be particularly effective in patients with disease of short duration. First, antagonism of TNF is effective for treating not only psoriasis and peripheral arthritis but also dactylitis, axial disease, nail involvement and enthesitis.^{48–51} Second, TNF blockade is associated with a rapid and dramatic decline in abnormal MRI signals, particularly those that indicate bone marrow edema, which, in RA, predict the development of erosive disease.⁵² Third, the presence of osteoclast precursors, which occurs in certain subsets of patients with psoriasis and PsA, correlates positively with erosive disease in PsA patients, and the level of these precursors declines significantly after anti-TNF treatment.^{53,54} Given the pivotal role of TNF in the pathogenesis of joint and periarticular inflammation, the identification of cellular or imaging biomarkers for arthritis in psoriasis patients might enable early treatment with TNF antagonists, and thereby delay or prevent the onset of musculoskeletal disease in psoriasis patients.^{55–57} The possibility that DMARDs have the same protective properties must also be considered, and clinical trials that include radiographic end points with these agents, particularly methotrexate, should be a high priority given the tremendous potential cost savings. However, additional studies that include imaging and cellular biomarkers need to be carried out to support this approach.

Treatment considerations

Data from placebo-controlled studies regarding the use of therapies in patients with PsA of short duration are not published; in addition, the availability of biologic agents—particularly anti-TNF agents—varies widely between countries. Nonetheless, a few general principles should be kept in mind when faced with treatment decisions (Box 2). It is essential that the clinician determines the full extent of the disease process. Treatment with sulfasalazine, even for mild peripheral arthritis, may not be appropriate in the presence of axial disease, and under-treatment of psoriasis can result in impaired quality of life and poor compliance. The need for specific imaging studies will be dictated by the results of clinical evaluation, but in most patients it is reasonable to obtain baseline radiographs of the hands, feet and anterior–posterior pelvis. The diagnosis of axial disease might require MRI, whereas enthesitis can be visualized

Box 2 | General principles for the treatment of early PsA

Identify the extent of musculoskeletal inflammation by use of:

- History and physical exam
- Plain radiographs
- MRI and/or Doppler ultrasonography

Diagnose comorbidities and tailor treatment accordingly.

Common comorbidities include:

- Uveitis and/or Crohn's disease
- Extensive cutaneous psoriasis
- Obesity, metabolic syndrome and diabetes
- Coronary artery disease

Simplify the treatment regimen, for example by decreasing the number of medications, to increase compliance

Avoid systemic corticosteroids

Monitor for progression of joint damage and functional loss with follow-up visits at least every 6 months, yearly radiography and close collaboration with the dermatologist

Abbreviation: PsA, psoriatic arthritis.

with both MRI and ultrasonography. Erosive disease can progress in the early stages of PsA, so radiography as well as other modalities (for example, MRI and ultrasonography) may be required to document joint damage in an effort to guide therapy.

The presence of comorbidities should also be documented so that appropriate interventions can be started and toxicities minimized. For example, weight loss, control of diabetes and hyperlipidemia, exercise and smoking cessation can all improve morbidity and mortality in this patient population. NSAID use should be avoided in patients with cardiovascular risk factors, as should the use of systemic steroids in all psoriasis patients because of their effects on lipids and atherogenesis and the possibility of a severe psoriasis flare (for example, erythroderma or pustular psoriasis) during drug taper. In addition, methotrexate would not be the optimal choice for patients with fatty liver, diabetes or heavy alcohol use.⁵⁸

From a compliance perspective, simplifying the treatment regimens is always preferred. Although efforts to combine topical agents with phototherapy and a DMARD might provide a favorable response, long-term compliance with these strategies is generally poor.⁵⁹ Also, the need to control both musculoskeletal and skin manifestations of the disease in an individual patient should not be underestimated; this challenging goal requires close collaboration between the dermatologist, rheumatologist and primary care physician. Serial monitoring for joint damage, metabolic risk factors and toxic effects of drugs are also imperative (and instrumental) in patients with early PsA.

Limited evidence exists to demonstrate the efficacy of NSAIDs and DMARDs in PsA, and scant data have been

published to show that these agents prevent radiological progression. Despite the lack of randomized controlled trials to demonstrate the efficacy of anti-TNF agents in the treatment of early PsA, it is reasonable to speculate that anti-TNF therapy may be extremely advantageous in this context. Anti-TNF agents are effective for treatment of the multiple manifestations of PsA, and result in a rapid decline in markers of joint damage in PsA. These benefits must, however, be weighed against the cost of instituting biologic therapy, although one recent study showed that the use of anti-TNF agents can be cost-effective within the first year of therapy.⁶⁰

Conclusions

Research over the past two decades has led to the appreciation that the majority of patients with PsA experience progressive joint destruction over a relatively short period of time. The fact that psoriasis precedes joint disease in most patients provides an opportunity to identify those patients most likely to develop arthritis. The concept of 'early PsA' is new, with little data on the feasibility of making an early diagnosis and no studies to date on the benefits of early therapy, and lags well behind the wealth of literature on early RA. The identification of patients early in the disease course is hampered by phenotypic heterogeneity and the absence of a diagnostic biomarker. Imaging studies have been of great benefit in early diagnosis of arthritis, especially

MRI and ultrasonography, which provide images of soft tissues and musculoskeletal structure. In addition, several questionnaires have been developed to help dermatologists screen patients with psoriasis for the presence of musculoskeletal disease.

Early treatment has the potential to alter the course of PsA, but evidence to support this statement is not yet forthcoming and will require a trial design similar to the BeST trial in RA.⁶¹ The possible advantages of early therapy further underscore the need for early diagnosis, but also point to the need for markers of poor prognosis that will help stratify treatment. Studies that measure biomarkers, assess advanced imaging modalities and perform validation of the available questionnaires in psoriasis patients are urgently required. Lastly, trials to demonstrate the efficacy of targeted biologic therapies and DMARDs in early PsA will test the validity of early intervention as a strategy to alter the disease course.

Review criteria

Published articles included in this Review were retrieved from a search of PubMed and the authors' collection of articles on psoriatic arthritis. Search terms used were "psoriasis", "psoriatic arthritis", "early psoriatic arthritis", "MRI", "ultrasound" and "treatment". The search was restricted to full-length articles, published in English-language journals since 2003.

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