Actas Dermosifiliogr. 2010;**101(9)**:742–748

ACTAS
Dermo-Sifiliográficas

Full English text available at
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REVIEW

Psoriatic Arthritis: What the Dermatologist Needs to Know, Part 2

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Manuscript received October 21, 2009; accepted for publication January 21, 2010

KEYWORDS
Psoriasis;
Psoriatic arthritis;
Evaluation methods;
Treatment

Abstract
This review aims to cover all aspects related to the treatment of psoriatic arthritis and the evaluation of the response to treatment. We define the various evaluation methods currently used to assess response to treatment in patients with psoriatic arthritis and the complementary examination techniques used to ensure adequate follow-up. These tools enable both the dermatologist and the rheumatologist to carry out an ongoing evaluation of the clinical course, severity, and prognosis of the disease. The treatment lines proposed by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis and the Spanish Society for Rheumatology are discussed. Emerging strategies for treating this condition and improving prognosis are examined.

PALABRAS CLAVE
Psoriasis;
Artritis psoriásica;
Métodos de evaluación;
Tratamiento

Artritis psoriásica. Lo que el dermatólogo debe saber (Parte 2)

Resumen
En esta revisión se pretenden abarcar todos los aspectos relacionados con el tratamiento de la artritis psoriásica así como la evaluación de la respuesta al tratamiento. Por este motivo, se definen los diferentes métodos de evaluación que se utilizan en la actualidad para valorar la respuesta al tratamiento de los pacientes con artritis psoriásica y las exploraciones complementarias que deben realizarse para el correcto seguimiento de estos pacientes. A través de estas herramientas, tanto el dermatólogo como el reumatólogo pueden evaluar la evolución, gravedad y pronóstico de la enfermedad en cada momento. En relación al tratamiento se exponen las líneas de tratamiento propuestas por la GRAPPA y la Sociedad Española de Reumatología (SER) y se introduce la aparición de nuevas terapias emergentes para el tratamiento de esta enfermedad y la mejora de su pronóstico.

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Evaluation Methods

The methods applied to evaluate psoriatic arthritis arose from the need to assess the activity of the disease at given moments during its course, the changes that emerge, and the impact of treatment. These methods enable us to understand the natural history of the disease and the effectiveness of treatment, yet while they are applied systematically in clinical trials, they are used less often in clinical practice. Given that brief fluctuations in disease activity are common in psoriasis, findings based on any evaluation method at a given time may not be pertinent to the patient's condition for long.

As well as evaluation methods, measures of function and quality of life are also important in this disease. The most widely used instruments are the Health Assessment Questionnaire (HAQ), which looks at loss of joint function, and the Short Form 36 Health Survey (SF-36), which is a specific tool for assessing quality of life.

Currently used tools have been adapted from others used in rheumatoid arthritis (Disease Activity Score [DAS]), spondyloarthropathy (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]), and psoriasis (Psoriasis Area and Severity Index [PASI]). The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the Outcome Measures in Rheumatology Clinical Trials (OMERACT)[1] group have proposed evaluation methods that can be used in clinical trials, although the only ones considered valid in daily clinical practice are the DAS in 28 joints (DAS-28) for rheumatoid arthritis and BASDAI for spondyloarthropathy. In order to increase specificity, new scales that incorporate objective data (eg, erythrocyte sedimentation rate (ESR) or C-reactive protein [CRP]) are being developed. One example is the Ankylosing Spondylitis DAS (ASDAS) endorsed by the Assessment of Spondylo/Arthritis International Society (ASAS) working group.[2]

These methods (Table 1) aim to evaluate the different domains of psoriatic arthritis, namely, the clinical, rheumatologic, cutaneous, and psychological aspects that affect patients with this disease and that must be evaluated and addressed individually. Through these means, the signs and symptoms of skin and joint involvement are evaluated, as are enthesitis, dactylitis, and spondylitis. Function, quality of life, fatigue, and structural changes (determined using plain radiography) are also evaluated.

Peripheral Joint Disease

The American College of Rheumatology (ACR) response indexes and improvement criteria and the DAS were developed to evaluate the activity of rheumatoid arthritis and are the approaches accepted by the European League Against Rheumatism (EULAR).

The ACR criteria consist of a count of affected joints based on 68 possible painful joints (distal and proximal interphalangeal, metacarpophalangeal, metatarsophalangeal, carpometacarpal, wrists, shoulders, elbows, acromioclavicular, sternoclavicular, hips, knees, talotibial, and mediotarsal) and 66 possibly inflamed joints (as above except for the hips [coxofemoral joints]). Both counts are scored from 1 to 3. The ACR20 (and the ACR50 or ACR70) response indexes detect 20% (and 50% or 70%) improvement in the affected joints. These criteria are known as the psoriatic arthritis response criteria (PsARC).[1]

The DAS was developed in Europe to evaluate the activity of rheumatoid arthritis and treatment-mediated changes in this disease. The advantage of the DAS over the ACR criteria is that the latter only measure changes in disease activity, whereas the DAS also makes it possible to evaluate the actual intensity of the disease at a given time, enabling the classification of patients into 3 groups: nonresponders, moderate responders, and good responders. The most commonly used instrument is the DAS-28, with a total count of 28 joints.[1]

As psoriatic arthritis affects other parts of the musculoskeletal system, as well as peripheral joints, below we summarize the evaluation criteria for axial disease, enthesitis, and dactylitis.

Axial Disease

The axial skeleton is affected in approximately 50% of patients with psoriatic arthritis, and in 25% of cases with sacroiliitis.

Diagnosis is based on the presence of 2 of the following criteria:

1. Inflammatory back pain (including age <45 years, duration of symptoms >3 months, morning stiffness >30 minutes, insidious onset, improvement with exercise, alternating pain in the gluteal muscles)

Table 1 Methods of Evaluation in Psoriatic Arthritis

Arthritis	Radiologic Criteria	Skin	QOL/ Functioning	Enthesitis	Dactylitis	Axial Involvement
ACR	Modified Van der Heijde/Sharp	PASI	SF-36	Leeds Enthesitis Index	Presence or absence	ASAS
PsARC			HAQ	SPARCC	Leeds Dactylitis Instrument	
DAS-28, DAS-44		PGA	DLQI	MASES		
			FACIT			

Abbreviations: ACR, American College of Rheumatology; ASAS, Assessment in Ankylosing Spondylitis; DAS, Disease Activity Score; DLQI, Dermatology Life Quality Index; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ, Health Assessment Questionnaire; MASES, Maastricht Ankylosing Spondylitis Score; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment of Psoriasis; PsARC, psoriatic arthritis response criteria; QOL, quality of life; SF-36, Short Form 36 Health Survey; SPARCC, Canadian Spondyloarthropathy Group, adapted from Mease.[5]

2. Limited cervical, thoracic, or lumbar movement in the sagittal and frontal planes
3. Radiologic criteria

Although axial disease is usually more variable and asymmetrical in patients with psoriatic arthritis than in those with ankylosing spondylitis, the evaluation criteria are usually the same and have been proposed by the ASAS. They include the BASDAI, the Bath Ankylosing Spondylitis Function Index (BASFI), and the Bath Ankylosing Spondylitis Metrology Index (BASMI).[1]

The instrument most commonly used in clinical practice is the BASDAI, under which disease is considered active when the score is 4 or more. When evaluating therapeutic response, the BASDAI should be applied 6 weeks after initiation of treatment. A response to treatment is indicated by a BASDAI score less than 3 or a reduction of 2 points.

Enthesitis

Enthesitis can be diagnosed using 3 approaches: ultrasound, magnetic resonance imaging, and physical examination and palpation (of the insertions of tendons, ligaments, and joint capsules).

The indexes used to evaluate enthesitis in spondyloarthropathy—and consequently in psoriatic arthritis—were developed to assess enthesitis in ankylosing spondylitis, although there is no consensus with regard to their use. These include the Mander Enthesitis Index (MEI), the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES), and the Major Enthesitis Index. The MEI evaluates 66 insertion points, whereas the MASES focuses on the 13 most important points included in the MEI. The MEI has a low yield: its inventory takes a long time to complete and it does not distinguish between points that are affected by psoriatic arthritis and points affected by fibromyalgia. The MASES was developed due to the need to obtain a simpler instrument with similar sensitivity. The Spondyloarthritis Research Consortium of Canada of the Canadian Spondyloarthropathy Group has created an index for enthesitis of the plantar fascia, Achilles tendon, tibial tuberosity, and the insertions of the rotator cuff.

Healy and Helliwell[3] proposed the Leeds Enthesitis Index, which was developed from the previous indexes, together with the Major Enthesitis Index and the Gladman Index. Therefore, it evaluates the insertions of the Achilles tendon, femoral medial condyles, and the lateral epicondyles of the humerus.[3] This index has the advantage over the others in that it only analyzes 6 points and can be administered quickly.

Dactylitis

Dactylitis is most commonly assessed in clinical practice by recording its presence or absence. A finding of dactylitis points to a high suspicion of psoriatic arthritis.

Additional Tests and Examinations

Although the diagnosis of psoriatic arthritis is basically clinical, it is important to perform additional studies if we are to evaluate the presence and degree of involvement of the different domains of the disease.

ESR and CRP

ESR and CRP are markers of inflammation. Persistently high serum levels of either or both of these markers in a patient with psoriatic arthritis indicate persistent inflammatory activity, even if the patient remains asymptomatic. In patients receiving treatment, changes in the levels of inflammatory markers can be used to monitor response to treatment, in such a way that persistently high levels indicate a lack of response.

Plain Radiography

To date, plain radiography is the only validated examination for assessing degree of joint involvement, disease progression, and response to therapy; however, it is not useful for evaluating involvement of musculoskeletal structures such as entheses, tendons, and ligaments. X-rays (Figure) to evaluate the degree of joint involvement are requested specifically according to symptoms and the results of the physical examination.

Ultrasound

When applied as an additional imaging test in psoriatic arthritis, ultrasound is particularly important in the evaluation of enthesitis, although its efficacy has not been established. Involvement of the plantar fascia is best observed using ultrasound. Similarly, power Doppler ultrasound can be used to evaluate the presence of synovitis in the affected joints, as well as the degree of vascularization of synovitis.

Magnetic Resonance Imaging

Magnetic resonance imaging is particularly effective at detecting involvement of the structures of the

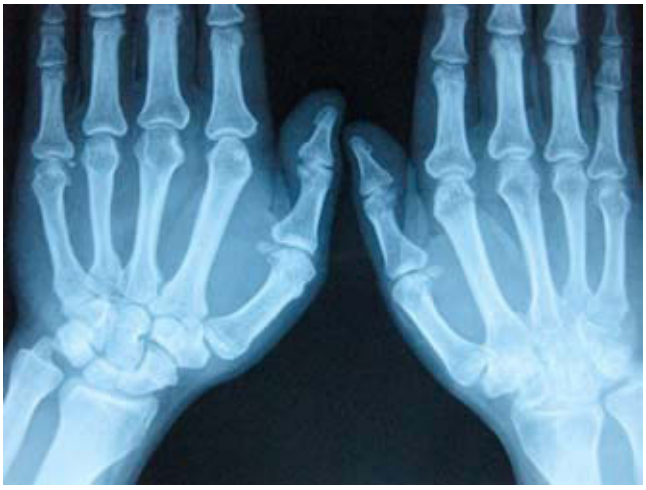

Figure Erosion on carpal bones visible on a plain radiograph of the right hand of a patient with psoriatic arthritis.

musculoskeletal system, although it has not been validated as a diagnostic tool in clinical practice. When enthesitis is suspected, magnetic resonance imaging detects associated bone edema and osteitis. Similarly, in joints that are difficult to examine, such as the sacroiliac joints, magnetic resonance imaging is extremely useful for detecting synovitis or erosions, thus confirming the initial diagnosis.

Clinical Course and Severity

The clinical predictors of a poorer prognosis for psoriatic arthritis are polyarticular involvement, elevated levels of acute phase reactants, evidence of erosive and osteophytic disease (with anatomic destruction and irreversible functional impairment), and lack of response to treatment.

Approximately 20% of patients with psoriatic arthritis progress to severe and debilitating forms that considerably affect quality of life and function.

In clinical practice, it is important to be able to classify a patient with psoriatic arthritis according to the severity of joint and musculoskeletal disease, taking into account the different domains of involvement. It is also important to establish the most suitable treatment for each patient and degree of severity. The GRAPPA has proposed an assessment battery of indexes described elsewhere, for example, the BASDAI and certain parameters the physician can evaluate during examination.[4] The GRAPPA method of classification is described in Table 2.

Prognosis

Factors associated with a poorer prognosis of peripheral joint disease are as follows: number of inflamed joints (polyarticular disease), elevated ESR, lack of response to treatment, presence of radiological abnormalities, loss of function (HAQ score), and reduction in quality of life (scores on the SF-36, Dermatology Life Quality Index, or Psoriatic Arthritis Quality of Life questionnaire).

Treatment

Treatment of psoriatic arthritis must take into account the different domains that make up this disease, since cutaneous and articular disease, as well as enthesitis, dactylitis, and spondylitis, may require a different therapeutic approach. Furthermore, the degree of involvement of each domain usually varies from patient to patient; therefore, treatment should be tailored.[5] Decisions on treatment should always take account of the domains expressed in a particular patient, in terms of functional involvement and disease-related quality of life.

Table 3 shows the GRAPPA recommendations for treatment.[4]

Although guidelines are generally similar in different countries and are drawn up using international consensus guidelines, there may be some variation between national health systems.

Current Criteria of the Spanish Society for Rheumatology

The consensus statement of the Spanish Society for Rheumatology proposes the following evaluation methods and activity criteria.[6]

Evaluation Methods

- Peripheral joint disease: painful and swollen joint count, overall evaluation by patient and physician, overall

Table 2 Levels of Severity of Psoriatic Arthritis According to the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis[a]

	Mild	Moderate	Severe
Peripheral arthritis	<5 joints No lesions on x-ray No loss of functioning Mild impact on QOL Patient evaluation: mild	≥5 joints Lesions on x-ray Moderate loss of function Moderate impact on QOL Patient evaluation: moderate	≥5 joints Severe lesions on x-ray Severe loss of function Severe impact on QOL Patient evaluation: severe
Skin disease	BSA <5, PASI <5, asymptomatic	No response to topical medication, PASI <10	BSA >10, DLQI >10, PASI >10
Axial disease	Mild pain No loss of function	Loss of function or BASDAI <4	No response to treatment
Enthesitis	1-2 points No loss of function	>2 points or loss of function	Loss of function or >2 points and loss of function
Dactylitis	No pain or moderate pain Normal functioning	Erosive disease or functional loss	Loss of response

[a]Adapted from Ritchlin et al.[4]

Abbreviations: BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; QOL, quality of life.

Table 3 Recommendations for Treatment According to the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

	Degree of Disease Severity	Treatment	Level of Evidence
Peripheral arthritis	Mild	NSAIDs	A
		Intra-articular corticosteroids	D
	Moderate/severe	DMARDs:	
		Sulfasalazine	A
		Leflunomide	A
		Methotrexate	B
		Ciclosporin	B
Skin disease	Moderate/severe	Phototherapy	A
		Methotrexate	A
		Fumaric acid esters	A
		Anti-TNF agents	A
		Ciclosporin	A
		Acitretin	A
		Alefacept	A
		Sulfasalazine	A
		Leflunomide	A
		Hydroxyurea	C
		Mycophenolate mofetil	C
		Thioguanine	C
Nail disease		Retinoids	C
		PUVA	C
		Ciclosporin	C
		Anti-TNF agents	C
Axial disease	Mild to moderate	NSAIDs	A
		Physiotherapy	A
		Education, sacroiliac analgesia and injections	A
	Moderate to severe	Anti-TNF agents	A
Enthesitis	Mild	NSAIDs, physiotherapy, corticosteroids	D
	Moderate	DMARDs	D
	Severe	Anti-TNF agents	A
Dactylitis		NSAIDs	D
		Corticosteroids	D
		DMARDs	D
		Infliximab	A

Abbreviations: DMARD, disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; PUVA, psoralen-UV-A; TNF, tumor necrosis factor.

evaluation of pain, acute phase reactants (ESR, CRP level, or both), physical function (HAQ), and evaluation of structural damage.
- Axial disease: BASDAI
- Enthesitis: MASES is the most widely accepted index for evaluating enthesitis in terms of number and locations.

Activity Criteria

- Polyarticular forms: The most widely used criteria in clinical trials are those of the DAS-28, the PsARC, and the ACR20, 50, and 70; however, these are not commonly used in clinical practice. The most widely used scale is the DAS-28, although it does not evaluate the distal interphalangeal joints or the joints of the feet. A DAS-28 score over 3.2 for more than 3 months is considered to indicate activity.
- Oligoarticular forms/enthesitis (≤4 locations): Activity is defined as arthritis, enthesitis, or both at 1 or more sites, together with at least 1 of the following: patient's evaluation of disease ≥4; increased acute phase reactants (ESR and/or CRP) for ≥3 months.

According to the Spanish Society for Rheumatology, therapy seeks to achieve remission, although this only occurs in a very small percentage of patients. Therefore, in patients with polyarticular involvement, a DAS-28 less than 2.6 (near remission) is considered acceptable; if this is not possible, low activity (<3.2) is acceptable. In oligoarticular forms, the objective should be to achieve complete resolution of inflammation in the affected joints, or if this is not possible, therapy aims to reduce the number of affected joints to fewer than 3, or a patient's report that fewer than 4 are involved; additionally or alternatively, achievement of a normal ESR or CRP value is a valid target.

Treatment should be reassessed in the case of persistent radiologic progression, isolated involvement of proximal or distal interphalangeal joints (or of any other site), and/or enthesitis that leads to marked functional impairment, as well as persistence of extra-articular manifestations such as uveitis or skin disease.

Indications for Biologics in the Treatment of Psoriatic Arthritis

Before biologics can be administered, the patient must have received appropriate treatment with a nonsteroidal anti-inflammatory drug (NSAID) and disease-modifying antirheumatic drugs (DMARDs) for articular forms and corticosteroid infiltrations for oligoarticular forms, dactylitis, or enthesitis. The recommended regimens for DMARDs, for which there is evidence of effectiveness in treating psoriatic arthritis, are as follows:

- Methotrexate: 7.5 mg/wk during the first month. Increase to 15 mg/wk at 1 month if arthritis persists and to 20-25 mg/wk the following month. Treatment should be changed after 2 months if there is no response to therapy with this dose.
- Sulfasalazine: 2-3 g/d for at least 3 months.
- Leflunomide: 20 mg/d for 3 months (10 mg/d in case of intolerance). An initial loading dose of 300 mg can be administered as 100 mg/d for the first 3 days followed by 20 mg/d.
- Ciclosporin A: 3-5 mg/kg/d for 3 months or the maximum tolerated dose.

Tumor Necrosis Factor α Antagonists

- Etanercept 50 mg/wk subcutaneously is as effective as 25 mg twice weekly for rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis.
- Infliximab: 5 mg/kg as an intravenous infusion at baseline, 2 weeks, and 6 weeks, followed by infusions every 8 weeks.[7]
- Adalimumab: 40 mg subcutaneously every other week.

These drugs can be administered alone or in combination with methotrexate, although there is insufficient evidence to say whether combination therapy increases or decreases efficacy.

All 3 anti–tumor necrosis factor α agents have been authorized for treating dermatological complaints based on their use in psoriatic arthritis. These agents all show similar efficacy in the treatment of psoriatic arthritis, leading to marked improvements in the PsARC, ACR criteria, and PASI. Although monoclonal antibodies (infliximab and adalimumab) are believed to be slightly more effective than etanercept at the beginning of treatment, results at 1 year are equivalent. Loss of efficacy over time is similar for all 3 drugs.

Therefore, infliximab, adalimumab, and etanercept can be used interchangeably in all the clinical domains of psoriatic arthritis, except dactylitis. Although all these drugs have led to clinical response in dactylitis, the only one authorized for treatment of this form is infliximab, at the doses reported above.[8-10]

Emerging Strategies

- Golimumab: This anti-TNF agent that is administered subcutaneously every month has proven to be significantly beneficial in the different domains of psoriatic arthritis.[11,12]
- Abatacept: Abatacept binds to CD80/86-presenting cells by blocking the interaction between T cells and CD28. Its efficacy in psoriatic arthritis is unknown.
- Denosumab: This osteoclastogenesis inhibitor inhibits the receptor activator for nuclear factor κ ligand[11] and is indicated to prevent or reduce osteoporosis.
- Certolizumab pegol: Certolizumab pegol is the first pegylated anti–TNF-α agent.

Objectives of Treatment: Minimal Disease Activity

Criteria for the definition of minimal disease activity in psoriatic arthritis were recently established. These criteria represent the objective of current treatments and are a useful tool for comparing approaches in clinical trials.[13] Any measurement criterion of the activity of psoriatic arthritis must include an evaluation of the different aspects involved, namely, peripheral joint disease, enthesitis, dactylitis, and spondylitis, as well as functional abnormality, and aspects related to quality of life. According to OMERACT, the parameters to be evaluated when determining the activity of psoriatic arthritis are peripheral joint disease, skin disease, pain, the patient's overall evaluation, physical function, and quality of life.

A patient is considered to have reached minimal disease activity on fulfillment of 5 of the following 7 criteria:

1. Number of painful joints ≤1
2. Number of inflamed joints ≤1
3. PASI ≤1 or body surface area ≤3
4. Pain on a visual analog scale ≤15
5. Patient's overall evaluation of disease activity ≤20
6. HAQ ≤0.5
7. Points of enthesitis ≤1

The definition of clinical remission in psoriatic arthritis has not yet been clearly established, and there is no consensus among authors. Some define remission as the absence of disease activity with regard to signs and

symptoms, whereas others consider it as the absence of activity in all disease domains. A suitable definition of remission must take account of any underlying disease, the consequences of this disease, and quality of life. In addition, the results of the tools for assessing the different domains of psoriatic arthritis must also be known.[8] While 20% of patients go on to develop destructive or disabling forms, other patients achieve remission. Gladman[14] defined remission as the absence of actively inflamed joints for 12 months and found that remission thus defined occurred in approximately 17.6% of cases. That study followed patients with psoriatic arthritis longitudinally for 20 years. Gladman also reported that mean time in remission was 2.6 years and that 52% of patients presented reactivation of the disease after this period.

Conclusions

Patients diagnosed with psoriasis who regularly visit their dermatologist to monitor their skin disease are usually seen to develop psoriatic arthritis at some point, and joint disease must be diagnosed and treated early to prevent progression of articular damage. Therefore, the dermatologist should be aware of the disease and the tools necessary to detect it. The dermatologist must also know when to refer the patient to a rheumatologist in order to ensure that the patient's condition is managed optimally.

Since the application of the Classification of Psoriatic Arthritis criteria, the dermatologist has taken on an important role in the diagnosis and management of this disease, as 2 of the lesser criteria are detection of active skin disease and recognition of signs of nail disease. Furthermore, therapeutic objectives in psoriatic arthritis currently envisage improvement in all clinical domains, including skin disease. Therefore, the dermatologist plays an important role in both diagnosis and follow-up, as well as in ensuring optimal treatment.

The rheumatologist's essential role is the preparation and application of tools to measure activity in most clinical domains of the disease, since optimal knowledge of psoriatic arthritis will enable more patients to have access to early treatment, thus halting disease progression.

Consequently, multidisciplinary teams are necessary for treating psoriasis and psoriatic arthritis. The presence of specialists with knowledge of the different aspects and comorbid conditions involved will ensure that the disease is controlled and that patients receive optimal therapy.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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