

# Current and relevant concepts in psoriatic arthritis

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## ABSTRACT

Psoriatic arthritis (PsA) is a systemic, polymorphic joint disease with variable presentation and clinical course. The outcome depends on the association with severe comorbidities such as diabetes, hypertension and dyslipidemia. Early diagnosis requires a high degree of clinical suspicion, especially when skin manifestations are subtle and poorly defined. Progressive erosive disease can occur in up to half of patients, associated with anatomical and functional changes in about 20%. Thus, the prognosis of PsA remains unclear, especially if diagnosis and treatment are delayed. Based on extensive literature review (PubMed and Lilacs) and experience of our services, new concepts of immunogenetics, pathophysiology, and clinical and therapeutic aspects are discussed. Factors that reduce the quality of life and life expectancy of patients, as well as new guidelines for treatment, will be emphasized. Control of inflammation, especially in enthesitis and axial forms of PsA, was made possible due to the introduction of anti-TNF biologics. Finally, the role of GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) should be emphasized, since it promotes meetings and joint studies between rheumatologists and dermatologists to provide scientific evidence for the sweeping changes in clinical management and treatment of patients with PsA.

**Keywords:** spondyloarthritis, psoriatic arthritis, arthritis.

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## INTRODUCTION

Psoriatic arthritis (PsA) was first reported by Louis Aliberti in 1818, when he noticed an association between psoriasis and arthritis. Currently PsA is recognized as an inflammatory joint condition associated with skin psoriasis and negativity for the rheumatoid factor. Thus, it can be distinguished from other types of arthritis essentially because of the concomitant presence of skin involvement. Two to three percent of the world population are considered to have isolated skin psoriasis, and arthritis might affect 5%–42% of those patients, depending on the geographical region and severity of the skin findings. The prevalence of PsA is estimated to be around 0.02%–0.25%. In approximately 75% of the cases, the skin condition precedes arthritis; in 15%, it appears after arthritis; and in 10%, the skin and articular involvements are simultaneous. Usually, skin involvement appears around the age of 15–35 years, while articular involvement appears two decades later. However, PsA is highly polymorphic, and can occur at any age, in adults and

children, although its incidence peaks around 40–50 years. Its frequency is similar in both genders, although males are more likely to have the spondylitic form (three to five times more). The skin disease can also be highly variable, assuming the following forms: psoriasis vulgaris; guttate psoriasis; inverse psoriasis; palmoplantar psoriasis; erythrodermic psoriasis; nail or scalp psoriasis.<sup>1–6</sup> It is worth noting that around 80% of patients with articular disease have nail involvement, sometimes subtle. Thus, patients with clinical suspicion of PsA should be carefully examined in search for signs of hidden psoriasis not only in the scalp, but also in the periumbilical, gluteal, and perianal regions, and mainly in the nails.

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) is an international entity created to promote educational and scientific meetings to foster the development and diffusion of information related to psoriasis and PsA among different medical experts working in the field, such as rheumatologists and dermatologists. Thus, it has been possible to boost research, diagnosis, follow-up, and treatment of psoriasis and PsA.

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## ETIOPATHOGENESIS

Although unknown and unexplainable,<sup>1-6</sup> the etiopathogenesis of PsA seems to be influenced by environmental, infectious and immunogenetic factors, because familial occurrence and presence of certain HLA antigens favor the manifestation of the articular disease.<sup>7-9</sup> In a genetically predisposed individual, environmental factors can trigger immunological alterations that will cause the disease. In fact, infections by viruses or Gram-positive bacteria, such as streptococcus, articular trauma, and emotional stress play important roles in the appearance of both skin psoriasis and articular disease. However, the possible neuro-immune-endocrine mechanisms involved in that process are yet to be clarified.

From the immunological point of view, changes are observed in both humoral and cellular immunity. The following have already been reported in affected individuals: circulating immune complexes; antibodies against antigens of the dermis and synovial membrane; and infiltrates of activated T lymphocyte subpopulations in the skin and synovial membrane. Undoubtedly, the identification of biomarkers will provide relevant information regarding susceptibility to the disease and its natural history, and can serve as a parameter for clinical follow-up and response to treatment. There has been evidence of genetic predisposition,<sup>10,11</sup> although there is no specific gene for the disease. Familial history of psoriasis is observed in 30%–50% of the patients. Investigation with twins has shown that both twins were subject to the disease in 65%–70% of monozygotic twins, and only in 30% of dizygotic twins.<sup>11</sup> That suggests the need for interaction with other factors.

In 1980, an association with HLA class I alleles (PSORS1) was established, and that with the HLA-Cw6 allele was the strongest. However, that allele, known as HLA-Cw\*0602 when identified through DNA typing, is present in 40%–80% of patients (and in 10%–15% of controls), with penetrance of around 10%, suggesting environmental effects or additional factors of genetic susceptibility. Regarding the clinical expression of the disease, Cw\*0602-positive patients initiate psoriasis at a younger age and have more severe and extensive skin disease, while nail changes and arthritis are more common in Cw6-negative patients. HLA-B27 can be present in 20%–60% of PsA patients, with increased incidence in the axial or spondylitic form, while DR4 is more commonly found in the erosive form, and DR7 and B38 in the peripheral involvement. Polymorphisms in the genes encoded in the HLA region of the 6p chromosome are associated with PsA. Other class I antigens (HLA-B13, HLA-B57, HLA-B39, HLA-Cw6, and HLA-Cw7) show a positive association in population studies

of psoriasis and PsA, and the association is stronger with HLA-Cw629. Some antigens seem to identify certain patterns of PsA, such as B27 associated with axial involvement of the disease, and B38 and B39 with peripheral polyarthritis. Other antigens were identified as prognostic factors, that is, B39 in isolation, B27 in the presence of DR7, or DQw3 in the absence of DR7 determine more severe disease in patients with PsA, while HLA-B22 seems to protect against disease progression. Other skin psoriasis susceptibility loci have been identified, such as PSORS2, PSORS3, PSORS4, and PSORS5. Genetic trait PSORS1-9 associated with PsA has favored the concept of a multifactorial genetic base, and that has been intensified with the discovery of more than 20 candidate *loci* associated with susceptibility for the disease and its expression by studies of linkage and genome-wide association scans (GWAS).<sup>12,13</sup>

Other genes implicated in psoriasis include SLC9A3R1, NAT9, RAPTOR, and SLC12A8, while CARD15 seems to predispose to PsA. Loci with recently confirmed association include HLA-C, three genes involved in IL-23 signaling (IL23A, IL23R, and IL12B), two genes that act on TNF-alpha and regulate NF-KB signaling (TNIP1 and TNFAIP3), and two genes involved in the modulation of Th2 immune response (IL4 and IL13).<sup>13</sup> Thus, the identification of several susceptibility loci involved indicates that psoriasis and PsA are genetically heterogeneous.<sup>14</sup> Proliferation of synoviocytes, infiltrates of inflammatory cells, such as T and B lymphocytes, and increased angiogenesis are evident. An infectious or environmental stimulus seems to act as a trigger, interfering with innate immunity and leading to the activation of keratinocytes and synoviocytes that recruit T cells to the damaged tissue, triggering PsA.<sup>15</sup>

The contribution of cell immunity to disease expression resulted from the observation that psoriatic patients with HIV infection had uncontrollable skin manifestations, asymmetrical polyarthritis, and marked nail dystrophy, possibly due to a deficiency in T helper cells (CD4).

Recent evidence has suggested that the inflammatory mechanism involves the activation of Th1 and Th17 response, with release of TNF, interferon (IFN), IL-23, IL-17, IL-22 and intercellular adhesion molecule 1 (ICAM1).<sup>16</sup> In the synovial tissue, serum, and psoriatic plaque, infiltrates of T lymphocytes and other inflammatory cells are observed, with increased expression of cytokines, such as TNF, IL-1, IL-6, and IL-18. Such findings, in addition to high serum levels of antibodies directed against staphylococci and streptococci, strengthen the notion that PsA could be a reactive process to the microbial flora present in the plaque in genetically susceptible individuals. TNF increase in the synovia, serum, and plaque of patients with PsA

confirms the relevance of the role of that pro-inflammatory cytokine in the pathogenesis of the disease. It also explains the significant therapeutic benefit achieved with the use of TNF blockers for controlling PsA clinical manifestations.

## CLINICAL ASPECTS

In 2006, the multicenter study CASPAR (Classification Criteria for Psoriatic Arthritis) developed new classification criteria for the diagnosis of PsA, which are currently used.<sup>17</sup> CASPAR was a multicenter prospective observational study, involving 30 centers and 13 countries, that assessed 1,012 consecutive patients diagnosed with PsA or other inflammatory arthritides. Clinician’s opinion was considered the gold standard for diagnosis. Those criteria provide better sensitivity than all the previous ones (91.4%), allowing the classification of earlier forms with limited expression, such as enthesitis and dactylitis, maintaining high specificity (98.7%). According to CASPAR, the establishment of the diagnosis of PsA requires the presence of peripheral or axial articular inflammatory disease or enthesitis with at least three points from the following features: evidence of skin psoriasis (current psoriasis was assigned a score of 2, while history of psoriasis or familial history of psoriasis were assigned a score of 1 each, as were all the other features), psoriatic nail dystrophy, rheumatoid factor negativity, dactylitis, and characteristic radiological evidence (Table 1).

**Table 1**  
CASPAR criteria for PsA<sup>17</sup>

To meet the CASPAR criteria for PsA, the patient should have inflammatory joint disease (peripheral, axial or enthesitis) and achieve three or more points, based on the following categories

<b>1. Evidence of psoriasis</b>	
Current	2 points
Personal history	1 point
Familial history	1 point
<b>2. Psoriatic nail dystrophy</b>	
Pitting, onycholysis, hyperkeratosis	1 point
<b>3. Negative test result for rheumatoid factor</b>	
	1 point
<b>4. Dactylitis</b>	
Current inflammation of an entire digit	1 point
History of dactylitis	1 point
<b>5. Radiological evidence of juxta-articular new bone formation</b>	
Well-defined ossification close to joint margins on plain radiographs of hands and feet	1 point

Sensitivity: 91%; specificity: 99%.

There is no characteristic pattern of articular or skin involvement in PsA. All patterns and degrees of arthritis can occur in patients with minimal skin lesions or with generalized exfoliative psoriasis.<sup>18–21</sup>

According to the initial description by Moll and Wright in 1973,<sup>22</sup> the articular manifestations of PsA were classified into five clinical forms or distinct subgroups: monoarticular or asymmetrical oligoarticular with dactylitis, in 70% of the patients; symmetrical polyarticular similar to rheumatoid arthritis (RA), in 25% of the patients; classical form, predominantly affecting the distal interphalangeal joints, in 5%–10%; arthritis mutilans, in 5%; and spondylitic form, in 5%–40% of the patients. Further studies<sup>23</sup> have shown a large variation in those incidences: 16%–70% for asymmetrical oligoarthritis; 15%–78% for the polyarticular form; 1%–17% for the classical form; 2%–16% for arthritis mutilans; and 2%–27% for the spondylitic form.

In fact, the results of those studies are in accordance with that observed at our services, where approximately 26% of the patients have oligoarthritis, 34% have polyarticular disease, 6% have the classical form, 8% have mutilating disease, and 26% have the axial form.<sup>24</sup>

The oligoarticular form of PsA is characterized by asymmetrical impairment of the proximal and distal interphalangeal and metacarpophalangeal joints, in addition to toes, ankles, knees, and hip joints. Digital arthritis and tenosynovitis often lead to dactylitis or the characteristic sausage digit. In symmetrical polyarthritis of the rheumatoid type, the articular manifestations involve small and large joints.

Radiological assessment shows the concomitant presence of erosive and proliferative lesions, resorption of distal tuft, bony ankylosis, “pencil in cup” deformity, and minimum periarticular osteopenia, all of them useful in the differential diagnosis.

Classical PsA affects the distal interphalangeal joints, and is usually accompanied by nail manifestations, such as transversal striae, pitting nails, and subungual hyperkeratosis.

Arthritis mutilans is the most severe form of the disease. It is destructive and involves preferentially fingers and toes, as well as metacarpophalangeal and metatarsophalangeal joints. It is associated with osteolysis of the phalanges involved, causing a deformity clinically known as “opera glasses” or telescoping fingers.

The spondylitic form of PsA affects as much as half of patients with PsA.<sup>21,23</sup> It is associated with the HLA-B27 antigen, and affects preferentially the axial skeleton, with a tendency towards asymmetrical sacroiliitis and presence of non-marginal syndesmophytes, also asymmetrical. Bilateral fusion of the sacroiliac joints can occur with disease progression.

Importantly, the joint involvement is very variable. Overlapping of manifestations between the several subgroups is frequent and the pattern of joint involvement can change as follows: patients with asymmetrical oligoarthritis can develop symmetrical polyarthritis over time. In addition, approximately 10%–50% of patients can have radiological changes in the sacroiliac joints, even when asymptomatic.<sup>23</sup>

For these reasons, the current trend is to classify PsA into three major clinical presentations: polyarticular, oligoarticular, and axial, which, at our services, correspond to 41%, 31% and 28% of patients, respectively.<sup>24</sup> While pulmonary fibrosis and aortic insufficiency are rare, the following extra-articular manifestations can occur:<sup>23</sup> conjunctivitis, in 20% of patients; uveitis, in 5%–10% of patients, mainly in axial disease; oral aphthae; and gastrointestinal involvement.

About 20% of the patients have a progressive course. Prognostic markers at the initial assessment are as follows: more than five swollen joints; an increase in acute phase proteins both at the beginning and in the course of disease; use of several different medications with persistence of polyarthritis; and accumulated joint damage between consultations. Other indicators of worse prognosis are the presence of familial history, extensive skin findings, beginning of disease before the age of 20 years, female gender, and specific genetic markers (HLA-B27 in the presence of HLA-DR7; HLA-B39 and DQw3 in the absence of DR7).<sup>25,26</sup>

The typical PsA patient can be either a male or female, who, around the age of 45 years and after any type of emotional stress, has erythematous and scaling skin lesions. Several months or years later, the patient develops inflammatory manifestations in the joints and adjacent soft tissues, with pain, swelling, and stiffness particularly in the fingers and toes. Physical examination reveals erythematous and scaling skin lesions associated with inflammatory arthropathy. Skin lesions can vary, being localized, diffuse, guttate or pustular. There is no specific skin involvement associated with a certain pattern of joint involvement. Thus, from minor skin lesions to severe generalized psoriasis can occur in patients with any pattern and degree of arthritis.

The only involvement that constitute a characteristic pattern is onychopathy associated with distal interphalangeal arthritis of the same finger,<sup>27</sup> which seems to result from the inflammation of the entheses closely related to the nail, joint and extensor tendon.<sup>28,29</sup> Laboratory assessment and complementary tests are unspecific,<sup>30,31</sup> and can exhibit elevation in acute-phase proteins, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and alpha-1-glycoprotein with polyclonal hypergammaglobulinemia. Anemia, hypoalbuminemia, mild

hyperuricemia, and circulating immune complexes can be present with normal or elevated serum complement. Antinuclear antibodies are present in up to 10% of cases, but IgM rheumatoid factor is absent. Synovial fluid analysis reveals an inflammatory pattern.

Severe erosive disease in distal interphalangeal joints, osteolysis with joint destruction, erosions, and bone proliferation and neoformation are typical radiological changes. Sacroiliitis can be unilateral in the initial phases, but it usually progresses to bilateral fusion. Isolated and asymmetrical syndesmophytes and signs of periostitis secondary to distal enthesopathy are characteristic of forms with axial involvement. Approximately 40%–50% of patients evolve to erosive arthritis and evident radiological damage.<sup>32–34</sup>

Pathological alterations in the entheses of patients with defined PsA and even of asymptomatic individuals have been demonstrated by the use of new modalities of diagnostic imaging techniques, such as magnetic resonance imaging (MRI) and ultrasonography (US).<sup>35–38</sup> Recent studies have reported the possibility of using US to monitor several aspects of PsA, including skin and nail lesions.<sup>39,40</sup> Although not yet totally defined, due to lack of methodological standardization, the role of the US and MRI seems promising for the initial and sequential assessment of these patients. The advantages US are easy access and low cost, enabling the assessment of the evolution of the alterations. Its disadvantages are being an examiner-dependent method and not properly standardized for PsA.

The identification of biomarkers<sup>9</sup> and the development of specific clinical instruments adequate for assessing patients with PsA, validated for clinical practice and clinical studies, are mandatory.<sup>30</sup> Biomarkers are extremely important in clinical practice, because they provide quantitative assessment during the diagnostic process, initial staging, and monitoring of both disease activity and response to treatment.<sup>9</sup> In PsA, different biomarkers can reflect genetic (Cw6 alleles), cellular (precursors of circulating osteoclasts) and inflammatory (CRP) involvements; the role of cytokines (TNF expression in the synovial tissue); and early alterations of bone lesion and imaging, revealing structural damage (bone edema on MRI).

The modulation of gene expression (MAP3K3, CACNA1S) and bone destruction (osteoprotegerin, DKK1) has been the focus of wide and intense investigation. Biomarkers of joint disease in individuals with skin psoriasis and joint damage in PsA are being developed thanks to the efforts of GRAPPA and OMERACT (Outcome Measures in Rheumatology Clinical Trials).

So far, well-defined criteria and instruments to assess PsA are still lacking. Thus, criteria and instruments developed for



other diseases, such as RA – improvement and response criteria of the American College of Rheumatology (ACR) and Disease Activity Score (DAS and DAS28) –, are used to assess PsA with peripheral involvement, as are those developed in clinical studies, but with no validation for the PsA population. Given the particularities of the disease, the response criteria used for RA may not be adequate for PsA.<sup>41,42</sup>

Psoriatic Arthritis Response Criteria (PsARC)<sup>43</sup> have been originally developed for a study of sulfasalazine in PsA, without previous adequate validation. Thus, specific indices comprising parameters of the entire spectrum of the pathology are required, being the reason of GRAPPA's great effort to improve the care of PsA. An ideal index should cover manifestations such as peripheral arthritis, sacroiliitis, spondylitis, enthesitis, dactylitis, and skin and nail diseases.<sup>30,44</sup>

Another important factor in managing PsA is that the entity, similarly to isolate skin psoriasis, is associated with a higher frequency of metabolic syndrome, increased cardiovascular morbidity and mortality,<sup>45–47</sup> and a relative reduction in life expectancy as compared with that of the general population.<sup>48–50</sup> Psoriatic individuals have increased prevalence of the traditional cardiovascular risk factors, such as diabetes mellitus, hypertension, dyslipidemia, smoking, obesity, and alcohol intake. In addition to reduced labor productivity, patients have higher levels of psychological stress and lack of satisfaction with their treatment. In a significant way, PsA leads to physical and mental functional disability, in addition to decreased quality of life, comparable to that of RA patients, depression, diabetes mellitus, and heart failure. Thus, preventive measures and careful control of modifiable cardiovascular risk factors and of the systemic inflammatory process are mandatory in those patients.<sup>51</sup>

## TREATMENT

An adequate therapeutic approach of PsA depends on the type and severity of the skin and joint involvements.<sup>52</sup> Based on comprehensive literature review and consensus opinion of 70 experts, including 54 rheumatologists and 16 dermatologists, Ritchlin *et al.*,<sup>52</sup> on behalf of GRAPPA, have established 19 recommendations regarding diagnosis, assessment and treatment of the five major clinical manifestations of PsA. Once established the diagnosis, the clinical form of arthritis and psoriasis should be characterized, aiming at providing the best treatment and final prognosis of the disease.<sup>53</sup> Early specific therapy should be initiated to prevent functional disability and provide better quality of life. Thus, treatment should be individualized and provided by a multiprofessional team (rheumatologists, dermatologists, psychiatrists, physical

therapists, occupational therapists, ophthalmologists, and psychologists). Physical measures combined with rehabilitation, physical therapy and occupational therapy are essential adjuvants, and, when necessary, corrective surgeries should be recommended. Maintenance of a program of physical activity, postural orientation, stretching exercises and muscle strengthening with the practice of isometric exercises should be encouraged and gradually initiated, as inflammation is controlled with medication.

Most patients, regardless of their form of joint involvement, show relief of symptoms with the use of different groups of non-steroidal anti-inflammatory drugs (NSAIDs).<sup>54</sup> Despite clinical benefits, data about the influence of NSAIDs in the clinical or radiological evolution of the disease are still lacking.

Systemic corticotherapy hinders the control of skin manifestations, and, thus, should not be used only routinely, and only for a limited period of time.<sup>55,56</sup> Systemic use of corticosteroids improves skin psoriasis, but their withdrawal triggers relapses in the form of “rebound effect”, producing recurrence of the skin manifestations or transformation into the generalized pustular form (von Zumbusch disease).<sup>55</sup>

Attention should also be paid to the intra-articular use of corticosteroids, because of the risk of joint contamination with bacteria present in skin psoriatic lesions, which require careful asepsis. The strategy of intra-articular infiltration can be useful to control pauciarticular cases or when the patient had a good response to therapy, but maintained a few inflamed joints. Rarely, in refractory systemic cases, intravenous pulse therapy can be used.<sup>57</sup>

Topical steroids for treating skin manifestations are subject to systemic absorption, producing desirable and undesirable effects.<sup>58</sup> Disease-modifying anti-rheumatic drugs (DMARDs) are indicated in patients who have neither rapid nor satisfactory response to NSAIDs, or in the presence of radiological or functional progression.

For controlling moderate to severe peripheral arthritis, the use of leflunomide or sulfasalazine is recommended according to studies with level of evidence A. Methotrexate (MTX) at adequate weekly doses remains a good therapeutic option for controlling both skin and peripheral joint disease (level of evidence 2a and 2b: one or more controlled clinical, non-randomized trials). Cyclosporine, azathioprine, colchicine, and mycophenolate mofetil represent other alternative possibilities.<sup>52–54</sup>

For skin manifestations, there is good level of evidence (recommendations 1a and 1b) for phototherapy, MTX, TNF-alpha inhibitors, efalizumab, cyclosporine, leflunomide, and sulfasalazine.<sup>52</sup> For axial manifestations, the following are recommended (1a/b): NSAIDs, physical therapy, analgesia,

sacroiliac infiltrations, and TNF-alpha inhibitors. For enthesitis, TNF-alpha inhibitors are recommended as first line therapy (1a), and NSAIDs and other DMARDs can be used.<sup>52</sup>

TNF-inhibitor biologics,<sup>59,60</sup> including infliximab,<sup>61</sup> etanercept,<sup>62</sup> adalimumab<sup>63</sup> and golimumab,<sup>64,65</sup> provide excellent long-term results, but are reserved for refractory cases. So far, there is no definitive international recommendation for the indication of anti-TNF agents in the treatment of PsA, although there are several national guidelines.

The following is usually recommended: correct diagnosis of the disease; at least three tender joints; resistant mono- or oligoarthritis of large joints or enthesitis; previous treatment failure with one to three slow-acting drugs for three to six months. In addition, evident effect should be observed after 12 weeks of treatment.<sup>66</sup>

In Brazil, according to the First Review of the Brazilian Consensus on Spondyloarthropathies,<sup>67</sup> the use of anti-TNF agents is recommended for patients with an inadequate response to the treatment with at least two slow-acting drugs for at least six months – in the case of MTX, the minimal dose of 25 mg/week should be achieved. A response is considered inadequate in the presence of joint activity in at least three tender and/or swollen joints, and can be associated with dactylitis or active skin disease.

It is worth noting that psoriasis can be an adverse event in individuals treated with anti-TNF agents, with no predisposing factor, and independent of the product used.<sup>68</sup>

Brazilian recommendations are in accordance with the procedures suggested by the GRAPPA,<sup>31,52,54</sup> which recommends the treatment of PsA according to the type of manifestation: skin and nails, peripheral arthritis, axial disease, dactylitis or enthesitis. For the skin disease, the use of specific measures, such as topical medications and PUVA/UVB, is recommended. Topical corticosteroids in combination with phototherapy can be sufficient to control mild skin disease, but systemic medication and even biologics can be necessary for extensive and refractory cases. Simultaneous dermatological assessment is fundamental to improve the management of psoriatic disease, since an adequate control of skin disease is important to manage arthritis. For the joint disease, NSAIDs, DMARDs, and, when necessary, anti-TNF agents are recommended. It is worth noting that anti-TNF agents are indicated in axial disease, enthesitis and dactylitis when the treatment with NSAIDs failed, emphasizing the scarce evidence on the efficacy of DMARDs in such cases.

For peripheral arthritis, GRAPPA recommends using DMARDs in monotherapy or in combination for at least three months, of which at least two months at standard target dose, although there is no evidence of efficacy of the combined therapy in PsA. In axial disease, a BASDAI decrease in six weeks suggests response to treatment. Biologics represent perspectives to the treatment of PsA. The anti-TNF golimumab and the anti-IL12/23 ustekinumab have shown improvement in dactylitis, enthesitis, and ACR 20.<sup>69</sup> Physical therapy and motor rehabilitation are important and should be stimulated in each phase of the treatment.

A study is underway with abatacept; and alefacept, an inhibitor of the activation of pathogenic T cells, provided a reduction in the synovial cellular infiltrate.<sup>70</sup> Surgical approach remains indicated for patients with sequelae and deformities due to the inadequate control of PsA. Thus, arthroplasties and other orthopedic interventions may be necessary. Post-operative care should be directed to the rapid joint mobilization, considering that PsA is a bone-forming arthropathy, and bone fusion in areas submitted to trauma can occur rapidly. However, with the recent discoveries and great advances in research due to the increment of biotechnology, we hope that, with the aid of specific biomarkers, the course of PsA can be altered to prevent the destructive progression of the disease, avoiding functional disability and improving significantly the quality of life of the patients affected.

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## CONCLUSION

Great advances in the investigation of the etiopathogenesis, clinical assessment and therapeutic approach of PsA have occurred. New classification criteria enabled the earlier diagnosis of affected patients. Progresses in the identification of biomarkers and imaging techniques, such as MRI and US, and the development of specific instruments of clinical assessment represent important perspectives on the diagnosis, follow-up and treatment of patients before the development of severe clinical manifestations. The recognition of risk factors for cardiovascular disease and their epidemiological importance will enable the increase in the patients' life expectancy. Finally, there is no doubt that the early diagnosis in conjunction with new forms of treatment directed at specific targets involved in the pathophysiology of the disease, such as anti-TNF-alpha agents, are improving dramatically the quality of life and prognosis of patients with PsA.

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