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2011 Consensus of the Brazilian Society of Rheumatology for diagnosis and early assessment of rheumatoid arthritis

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ABSTRACT

Objective: Develop guidelines for management of rheumatoid arthritis (RA) in Brazil, focusing on diagnosis and early assessment of the disease. **Method:** Literature review and expert opinions of RA Committee members of the Brazilian Society of Rheumatology. **Results and conclusions:** The following ten recommendations were established: 1) RA diagnosis should be established considering clinical findings and complementary test results; 2) Special attention should be given to the differential diagnosis of arthritis; 3) Rheumatoid factor (RF) is an important diagnostic test, but has limited sensitivity and specificity, mainly in early RA; 4) Anti-CCP (anti-cyclic citrullinated peptide antibody) is a marker with sensitivity similar to that of the RF, but with higher specificity, mainly in the initial phase of disease; 5) Although unspecific, acute-phase reactants should be measured in patients with clinical suspicion of RA; 6) Conventional radiography should be performed for diagnostic and prognostic assessment of the disease. When necessary and available, ultrasound and magnetic resonance may be used; 7) Rheumatoid arthritis classification criteria (ACR/EULAR 2010), although not yet validated, may be used as a guide to aid in diagnosing patients with early RA; 8) One of the combined disease activity indices should be used to assess disease activity; 9) At least one of the functional capacity assessment instruments, such as mHAQ or HAQ-DI, should be regularly used; 10) At the early assessment of the disease, the presence of worse prognostic factors, such as polyarticular involvement, high titers of RF and/or anti-CCP, and early joint erosion, should be investigated.

Keywords: rheumatoid arthritis, diagnosis, assessment, consensus.

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INTRODUCTION

Rheumatoid arthritis (RA) is a systemic, chronic and progressive inflammatory disease that affects mainly the

synovial membrane of joints, leading to bone and cartilaginous destruction.¹

The condition affects 0.5% to 1% of the adult population worldwide, and can occur in all ethnic groups.² Rheumatoid

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arthritis predominates in females (two to three times more common) and affects mainly patients in their fourth to sixth decades of life, but has been reported at all age groups.³

A Brazilian multicenter study of population samples from Brazilian macroregions (North, Northeast, West-central, and South) has reported RA prevalence of up to 1% in the adult population,⁴ corresponding to an estimate of 1,300,000 people affected.

Rheumatoid arthritis is a chronic disease, with an irreversible joint damage potential, resulting in high costs to affected individuals and society.⁵⁻⁷

The understanding of RA pathophysiology, its diagnostic methods and therapeutic management have undergone considerable advances in recent years, particularly regarding the initial period of the disease, the so-called early RA (first 12 months of RA symptoms), recognized as a therapeutic “window of opportunity”.⁸⁻¹⁰ Despite these advances, the current diagnostic and prognostic indicators (clinical, laboratory, and radiographic) play a limited role in early RA diagnosis and establishment of individual prognosis.¹¹

The demographic and clinical characteristics of RA vary according to the population affected.¹² Most information available originates from Europe and the United States.^{13,14} Studies conducted in the Brazilian population are scarce.^{15,16}

Rheumatoid arthritis affects patients in their productive years and may provide significant limitation in their functional capacity, in addition to labor capacity loss; thus, the indirect costs related to these factors should be incorporated into pharmacoeconomic analyses.¹⁷

In Brazil, as well as in developed countries, RA-related costs are high.¹⁸ Such costs have greater repercussion in developing countries, whose financial resources for health are less robust. This emphasizes the need for studies assessing RA costs and allocation of resources for RA diagnosis and treatment adapted to the Brazilian reality.¹⁹

METHOD FOR ELABORATING THE CONSENSUS

The present consensus was aimed at elaborating guidelines for RA management, with an emphasis on disease diagnosis, considering peculiar aspects of the Brazilian socioeconomic reality.

The method for elaborating the consensus for the development of guidelines includes literature review and the opinion of experts, who are members of the Rheumatoid Arthritis Committee of the Brazilian Society of Rheumatology (SBR). The bibliographic survey comprised publications existing in the MEDLINE, SciELO, PubMed, and EMBASE databases up to March 2011. The guidelines were written and reassessed by all participants during three meetings held in October 2010,

December 2010, and February 2011, in addition to several rounds of questioning and corrections carried out via Internet.

DIAGNOSIS

The diagnosis of RA should be established considering the clinical findings and complementary test results. No isolated test, either laboratory, imaging, or histopathological, confirms the diagnosis.

Table 1
Differential diagnosis of arthritis

Groups of diseases	Diseases
Infections	Viral (dengue, HIV, parvovirus, cytomegalovirus, hepatitis virus), bacterial (<i>N. gonorrhoeae</i> , <i>S. aureus</i>), mycobacterial, fungal, etc.
Spondyloarthritides	Reactive arthritides (<i>Chlamydia</i> , <i>Salmonella</i> , <i>Shigella</i> , <i>Yersinia</i>), ankylosing spondylitis, psoriatic arthritis, enteropathic arthritides
Systemic rheumatic diseases	Systemic lupus erythematosus, polymyositis/dermatomyositis, systemic sclerosis, Sjögren syndrome, Behcet disease, rheumatic polymyalgia, systemic vasculitides, etc.
Microcrystal arthritides	Gout, calcium pyrophosphate crystal deposition disease, etc.
Endocrine disorders	Hypothyroidism, hyperthyroidism
Neoplastic diseases	Metastatic neoplastic diseases, lymphoma, paraneoplastic syndromes, etc.
Others	Osteoarthritis, hemochromatosis, amyloidosis, sarcoidosis, serum disease, angioedema

Arthritis can be part of the course of several diseases, which, thus, should be considered in the differential diagnosis with RA,^{20,21} as shown in Table 1.

When RA presents in its definite form, with all its typical findings, its recognition is easier. Diagnosing the disease in its early phase, however, may be difficult, because characteristic serological and radiographic alterations are often missing.²²

The clinical manifestations of RA can be divided into articular and extra-articular. Because RA is a systemic disease, general symptoms such as fever, asthenia, fatigue, myalgia, and weight loss may precede or accompany the onset of articular manifestations.²³

ARTICULAR MANIFESTATIONS

Articular manifestations of RA may be reversible in its early stages. However, when joint destruction has already occurred, the alterations caused by persistent synovitis, bone and cartilage destruction, loss of mobility, and muscle, tendon and ligament changes are irreversible.

The basic characteristic of the articular manifestation of RA is synovial inflammation (synovitis), which can affect any of the diarthrodial joints of the body.

The clinical complaint comprises pain, swelling, and reduced range of motion in affected joints. On physical examination, there are joint tenderness, increased joint volume, intra-articular effusion, joint warmth, and, occasionally joint redness. Deep joints, such as hips and shoulders, may not evidence these findings.²³

The characteristics of arthritis in RA are as follows:²³

- a) *Polyarticular involvement*: usually more than four joints are involved. However, the disease may begin and persist as mono- or oligoarthritis.
- b) *Arthritis in wrists and hands*: the involvement of wrists, metacarpophalangeal (MCP) joints, and proximal interphalangeal (PIP) joints is frequent since disease onset. The distal interphalangeal (DIP) involvement is rare, which is useful in differentiating RA from other conditions, such as osteoarthritis and psoriatic arthritis.
- c) *Symmetrical arthritis*: symmetrical joint involvement is common, although in case of PIP, MCP, and metatarsophalangeal (MTP) joints, symmetry is not necessarily complete.
- d) *Cumulative or additive arthritis*: arthritis usually has a cumulative pattern (progressively involves new joints, but keep the previously affected inflamed).
- e) *Morning stiffness*: prolonged morning stiffness, characterized by joint stiffness and swelling, identified mainly in the morning, is an almost universal finding of synovial inflammation. Unlike the brief stiffness observed in osteoarthritis (usually five to ten minutes), in inflammatory diseases, stiffness lasts more than one hour. This phenomenon is associated with reduction in motion occurring during sleep or rest and not with the time of day. Duration tends to correlate with the degree of inflammation, and is a parameter that should be documented for disease follow-up.^{24,25}

EXTRA-ARTICULAR MANIFESTATIONS

Although articular manifestations are the major characteristics, RA can affect other organs and systems. The most frequent extra-articular manifestations include cutaneous, ocular, pleuropulmonary, cardiac, hematologic, neurological, and osteometabolic findings. They are more common in patients with severe and polyarticular disease, positive serology for rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibody (anti-CCP), and rheumatoid nodules.^{26,27}

Brazilian studies have confirmed the following as early manifestations of RA: polyarticular involvement; persistent synovitis in the hands; prolonged morning stiffness; high number of tender and swollen joints; and fatigue.^{15,16}

LABORATORY TESTS

Acute phase response measurements

The most commonly used laboratory markers for assessing RA activity are the following acute-phase reactants: erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).²⁸ Erythrocyte sedimentation rate is usually measured using the Westergren method (mm/first hour), and CRP is mainly measured by quantitative method (in mg/dL or mg/L).

Although such tests are often requested during follow-up and might correlate with the periods of disease activity, they are not specific. Erythrocyte sedimentation rate and CRP vary according to age and sex, and ESR can be influenced by several variables, such as hemoglobin levels, pregnancy, hypoalbuminemia, and hypofibrinogenemia.²⁹

In a Brazilian cohort of early RA, more than two thirds of patients assessed had elevated acute-phase reactants (ESR and CRP) at baseline.³⁰

Autoantibodies

Some autoantibodies, such as RF and several anti-citrullinated protein/peptide antibodies (ACPA), including anti-CCP, act as RA potential diagnostic markers.³¹

Rheumatoid factor

Rheumatoid factor is an autoantibody directed against the Fc portion of IgG.³² It is classically associated with RA, detected in serum of approximately 70% of patients, and correlates statistically with worse prognosis. Higher titers are associated with aggressive disease, presence of rheumatoid nodules, and extra-articular manifestations.³¹

Individually, the diagnostic value of RF is limited, because 30% to 50% of patients, at disease onset, can be seronegative for this autoantibody.³² In addition to low sensitivity, the test specificity is also limited. RF may be positive in the absence of arthritis, with increased prevalence with aging,³³ and may still be present in several other conditions, either rheumatologic or non-rheumatologic.^{34,35} Thus, a negative RF test does not exclude the diagnosis of RA, and its positivity should be carefully interpreted according to clinical findings.

Brazilian data (incident cohort of early RA) have shown a prevalence of RF in approximately 50% of patients.³⁰

Anti-citrullinated protein/peptide antibodies

Recently, several ACPA have emerged as important diagnostic tools for RA, with sensitivity similar to and specificity greater than that of RF, besides having a possible role in the pathogenesis of disease.³⁶ Their role as possible RA activity markers is controversial.³⁷

Anti-cyclic citrullinated peptide antibodies

Among the antibodies directed against antigens of filaggrin-citrulline system studied, the anti-CCP antibodies have shown the greatest clinical applicability. The test sensitivity is 70%-75%, its specificity is approximately 95%, and it is particularly useful in the subgroup of patients with early arthritis and negative RF.³⁸

Its investigation is valid in assessing undifferentiated arthritis. The anti-CCP antibodies are detected very early in the course of RA and can be used as an indicator of RA progression and prognosis.³⁹⁻⁴⁸

Other antibodies

Other autoantibodies have been used in RA investigation. The objective is to develop methods with sensitivity and specificity for earlier RA diagnosis, more reliable activity markers, and prognostic indicators. Some of the autoantibodies used in RA investigation are as follows: mutated citrullinated vimentin antibodies (anti-MCV);⁴⁹⁻⁵¹ antikeratin antibodies (AKA); anti-perinuclear factor (APF);⁵² antifilaggrin autoantibodies;⁵³ anti-human citrullinated fibrinogen antibodies (ACF);⁵⁴ anti-heterogeneous nuclear ribonucleoprotein A2 autoantibody (anti-RA33);⁵² anti-interleukin 1 antibody (anti-IL1);⁵⁵ anti-alpha-enolase antibody;⁵⁶ and anti-advanced glycation end-products antibody.⁵⁷ These antibodies have, in general, good specificity, but sensitivity lower than that of anti-CCP for diagnosing RA.

The recent criteria for classifying RA,⁵⁸ jointly established by the American College of Rheumatology (ACR) committee and the 2010 European League Against Rheumatism (EULAR), have defined in the "autoantibodies" item only RF and ACPA. According to these criteria, the RF or ACPA levels have been established as negative, and low- and high-positive. Considering that both RF and anti-CCP are measured in IU, the result is considered negative when the value found is \leq the upper limit of normal (ULN) for the laboratory and assay; low-positive, when the result is $>$ the ULN, but \leq three times the ULN; and high-positive when the value found is $>$ three times the ULN.

Genetic assessment

Several genetic markers have been described associated with the occurrence of RA. However, the only well-established genetic alteration associated with RA, with a strong level of evidence, has been the identification of HLA-DRB1 alleles (presence of shared epitope) and of PTPN22 genes.⁵⁹ The interaction between HLA-DRB1, smoking, and anti-CCP determines a more severe disease profile of worse prognosis. However, although useful for characterizing patients with worse prognosis, the high costs of HLA-DRB1 typing still limit its use in daily practice.^{59,60}

IMAGING TECHNIQUES

Conventional radiography

Conventional radiography is the most used imaging technique for assessing the structural joint damage in RA. In addition to being useful for diagnosis, it is important when repeated at regular intervals to monitor disease progression.⁶¹

The initial radiographic findings include enlarged juxta-articular soft tissues and osteopenia. The most characteristic lesions, such as a reduction in the joint space and bone erosions, appear later.

The presence of bone erosion should be considered a risk factor for development of persistent arthritis when observed in early disease.⁶² It relates to functional limitation, and, consequently, to worse prognosis.⁶³

Ultrasound

The sensitivity of musculoskeletal ultrasound and magnetic resonance in detecting structural joint damage is greater than that of conventional radiography.⁶⁴

Ultrasonography, when performed by an expert in musculoskeletal diseases, is useful for the early detection and monitoring of inflammatory activity and signs of joint destruction.⁶⁵

When compared to magnetic resonance, it is a less expensive exam, and not contraindicated for patients with metallic implants or claustrophobia. Moreover, it allows a dynamic joint examination, a comparative contralateral assessment, as well as the assessment of other anatomic structures.⁶⁴⁻⁶⁷

The use of power Doppler and color Doppler can complement the exam and aid in characterizing inflammatory activity.⁶⁸

Magnetic resonance

Magnetic resonance is the most sensitive method to detect early RA alterations. It allows the assessment of structural changes

Table 2
Advantages and disadvantages of imaging techniques used to assess RA patients

Techniques	Advantages	Disadvantages
Conventional radiography	- Low cost - Easy access	- Two-dimensional representation of three-dimensional lesions - Exposure to ionizing radiation - Low sensitivity to early bone damage
Ultrasound	- Intermediate cost - No ionizing radiation - Allow assessment of several joints - Provides guidance for diagnostic and therapeutic interventions - Detection of early bone and cartilaginous structural damage - Detection of inflammatory activity by use of power Doppler	- Operator-dependent exam - Low sensitivity to detect deep joint changes (hips)
Magnetic resonance	- High sensitivity - No ionizing radiation - Complementation of the exam with contrast medium - Detection of bone edema, and early bone and cartilaginous structural damage	- High cost - Limited availability of the equipment - Long exam duration - Limited to one joint per exam (knee, hand)

in soft tissues, bones, and cartilages, in addition to erosions, prior to conventional radiographies.⁶⁹

In addition to RA conventional radiographic findings, magnetic resonance can detect bone edema, which proved to be a predictor of bone erosion.⁶⁵

In Brazil, factors such as its high cost and method standardization have limited its use in clinical practice.

Table 2 shows the advantages and disadvantages of the imaging techniques used to assess patients with RA.

Other imaging techniques

Other imaging techniques, such as bone scintigraphy and computed tomography, are not currently recommended for RA diagnosis.⁷⁰⁻⁷²

NEW CLASSIFICATION CRITERIA OF RA

RA classification has been essentially based on criteria introduced by the ACR in 1987,⁷³ and shown in Table 3, which are not suitable for early RA.⁷⁴ The ACR classification criteria for

Table 3
1987 American College of Rheumatology Criteria for rheumatoid arthritis classification

Criterion	Definition
1) Morning stiffness	Morning stiffness in and around the joints, lasting at least one hour before maximal improvement
2) Arthritis of three or more joint areas	At least three joint areas simultaneously have had soft tissue swelling or fluid observed by a physician (PIP, MCP, wrist, elbow, knee, ankle, and MTP joints)
3) Arthritis of hand joints	At least one area swollen in a wrist, MCP, or PIP joint
4) Symmetric arthritis	Simultaneous involvement of the same joint areas on both sides of the body
5) Rheumatoid nodules	Subcutaneous nodules, over bony prominences, or extensor surfaces, or in juxta-articular regions
6) Serum rheumatoid factor	Demonstration of abnormal amounts of serum rheumatoid factor
7) Radiographic changes	Posteroanterior hand and wrist radiographs showing juxta-articular bony decalcification or erosions

For classification purposes, a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least four of these seven criteria. Criteria one through four must have been present for at least six weeks. Modified from Arnett *et al.*⁷³

RA were developed based on individuals with long-term RA, and were considered the standard for selecting patients for clinical studies. Such criteria have sensitivity of 91%-94% and specificity of 89% for established RA. However, they include characteristics less frequent in RA of recent onset, such as radiographic alterations (erosions) and rheumatoid nodules, being considered suboptimal for identifying individuals with early RA (sensitivity of 40%-90% and specificity of 50%-90%).⁷⁵

Therefore, it became necessary to establish new criteria for RA classification, especially focusing on the early stage of disease.⁵⁸

The ACR/EULAR new RA classification criteria can be applied to all patients, as long as they meet the two basic requirements:

- 1) have at least one joint with definite clinical synovitis at the time of assessment;
- 2) the criteria may be applied only to those patients for whom the observed synovitis is not better explained by another diagnosis.

The criteria proposed (Table 4) are based on a scoring system of direct sum. The manifestations are divided into four domains: joint involvement, serology, duration of symptoms, and acute-phase reactants. Affected joint count can use imaging techniques (ultrasound and magnetic resonance) in case of doubt. A score ≥ 6 classifies a patient as having RA.⁵⁸ The criteria can be fulfilled in a prospective or retrospective way, in the presence of adequate recording.

Table 4
2010 ACR/EULAR Classification Criteria for RA

Target population (who should be tested?)	
Patients with definite clinical synovitis (swelling) in at least one joint.* The observed synovitis is not better explained by another diagnosis. *The differential diagnoses can include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. In case of doubts regarding the relevant differential diagnoses, a rheumatologist should be consulted.	
Joint involvement (0-5)	
1 large joint	0
2-10 large joints	1
1-3 small joints (large not counted)	2
4-10 small joints (large not counted)	3
> 10 joints (at least one small joint)	5
Serology (0-3)	
Negative RF and negative ACPA	0
Low-positive RF or low-positive ACPA	2
High-positive RF or high-positive ACPA	3
Duration of symptoms (0-1)	
< 6 weeks	0
≥ 6 weeks	1
Acute-phase reactants (0-1)	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1

A score of ≥ 6 is needed for definitive classification of a patient with RA.

Joint involvement refers to any swollen or tender joint on examination (distal interphalangeal joints of hands or feet, first metatarsophalangeal joints and first carpometacarpal joints are excluded from assessment). Further evidence obtained through imaging techniques can be used for confirming clinical findings. For the purpose of classification, **small joints** refers to *metacarpophalangeal joints, proximal interphalangeal joints, metatarsophalangeal joints (second through fifth), first interphalangeal joints, and wrists, and large joints* refers to *shoulders, elbows, hips, knees, and ankles. Additional joints (e.g., temporomandibular, sternoclavicular, acromioclavicular)* can be counted in the "more than 10 joints" assessment, as long as at least one small joint is involved.

In the **serology domain**, the result of the rheumatoid factor or anti-citrullinated protein/peptide antibodies is considered negative if the values found are ≤ the upper limit of normal (ULN) for the laboratory and assay; low-positive, when the result is > the ULN, but ≤ three times the ULN; and high-positive when the value found is > three times the ULN.

The **duration of symptoms** domain refers to patient self-report of maximum duration of signs and symptoms of any joint that is clinically involved at the time of assessment.

The **acute-phase reactants** (erythrocyte sedimentation rate and C-reactive protein) are considered normal/abnormal according to local laboratory standards. Modified from Aletaha et al.⁵⁸

It is worth noting that, if a patient has a history consistent with RA, even in the absence of documentation, and typical radiographic erosions, the patient can be directly classified as having RA, regardless of meeting the criteria.⁵⁸

The new 2010 criteria are not *diagnostic*, but *classifying*. Their function is basically defining homogeneous populations for studies.

The clinical diagnosis is extremely complex and comprises several aspects that can hardly be summarized in the form of a scoring criteria.⁵⁸ Occasionally, formal criteria can serve as a guide for establishing clinical diagnosis.

Several aspects regarding the new criteria need to be carefully analyzed before they are universally accepted. However, these criteria must be validated in different populations, including Brazilian cohorts of early RA.

DISEASE ACTIVITY ASSESSMENT

Once established the diagnosis of RA, its prognostic factors, and the occurrence of comorbidities, it is important to characterize parameters useful for adequately monitoring disease activity still in the early assessment of RA.

Some validated parameters that correlate with RA activity are as follows: patient visual analogue scale regarding pain; patient and physician visual analogue scale regarding disease activity; number of tender and swollen joints; instruments for assessing functional capacity (such as the Health Assessment Questionnaire - HAQ); acute phase reactants (ESR and/or CRP); fatigue; duration of morning stiffness; radiography of the hands, wrists and feet; quality of life indices, such as, the 36-Item Short Form Health Survey (SF-36).⁷⁶⁻⁸¹

Through these parameters, combined disease activity indices have been created and validated. The major indices are as

Table 5
Calculation and total value of the combined disease activity indices

Elements	SDAI	CDAI	DAS28 (with 4 variables)
Number of swollen joints	(0-28) Simple sum	(0-28) Simple sum	Square root of the simple sum
Number of tender joints	(0-28) Simple sum	(0-28) Simple sum	Square root of the simple sum
Acute-phase reactants	CRP (0.1 - 10 mg/dL)	—	ESR 2-100 mm or CRP 0.1-10 mg/dL logarithmic transformation
Global health assessment (patient)	—	—	0-100 mm
Disease activity assessment (patient)	(0-10 cm)	(0-10 cm)	—
Disease activity assessment (physician)	(0-10 cm)	(0-10 cm)	—
Total index (index range)	Simple sum (0.1-86)	Simple sum (0-76)	Requires inserting number in the calculator (0.49-9.07)

SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score (28 joints); CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate. (ESR range: 2 to 100 mm/h; CRP range: 0.1 to 10 mg/dL).

follows: Disease Activity Score in 28 joints (DAS28); Simplified Disease Activity Index (SDAI); and the Clinical Disease Activity Index (CDAI). These indices use a more simplified count of 28 joints (PIP, MCP, wrists, elbows, shoulders, and knees, bilaterally) and determine a numerical value for RA activity. Tables 5, 6, and 7 show how to calculate and use such indices.⁸²⁻⁹¹

There is a good correlation between these combined disease activity indices (CDAI, SDAI and DAS28), and any of them can be used in isolation. Patients undergoing remission or low disease activity, according to any of these indices, also have slower radiographic progression, and better functional evolution. Thus, patients should always be kept in clinical remission, or, if this is not possible, at least in a state of low disease activity.⁸³

QUALITY OF LIFE AND DISABILITY

Assessing quality of life and disability in RA is of major importance to better understand the disease course.⁹²

Table 6
Cutoff points of the combined disease activity indices according to RA activity

Index	Disease activity status	Cutoff points
SDAI	Remission	≤ 5
	Low	> 5 and ≤ 20
	Moderate	> 20 and ≤ 40
	High	> 40
CDAI	Remission	≤ 2.8
	Low	≤ 10
	Moderate	> 10 and ≤ 22
	High	> 22
DAS28	Remission	≤ 2.6
	Low	> 2.6 and ≤ 3.2
	Moderate	> 3.2 and ≤ 5.1
	High	> 5.1

SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score (28 joints); modified from Aletaha *et al.*⁸³

Table 7
Response according to the score variation of the combined disease activity indices

Index	Type of response
EULAR - DAS28 Response ⁸⁹⁻⁹⁰	Good: decrease > 1.2 points, and patient reaching DAS28 with low activity (< 3.2) Moderate: decrease of 1.2 points in DAS28; decrease between 0.6 and 1.2 points, with a reduction in disease activity from high to moderate or from moderate to low
SDAI Response ⁹¹	Good: decrease of 17 points Moderate: decrease of 7 points
CDAI Response ⁹¹	Good: decrease of 14 points Moderate: decrease of 6 points

SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score (28 joints); modified from Aletaha *et al.*⁹¹

Rheumatoid arthritis, even in its early phase, can cause considerable impact on health-related quality of life (HRQoL).⁹³ HRQoL is a very wide concept, which can be simplified as the impact of health on the individual's functional ability and well-being perceived in the physical, mental, and social life domains.⁹⁴

Several instruments have been proposed aimed at assessing the quality of life of patients with RA, detecting changes in the health status over time, and at assessing the prognosis, risks and benefits of a certain therapeutic intervention, including generic and specific instruments.⁹⁵⁻¹¹⁶ The most used are the HAQ, including the modified (mHAQ) and the disability index (HAQ-DI) versions, in addition to the SF-36.

Studies in a Brazilian cohort of early RA have shown an important impact on quality of life at the time of diagnosis, according to assessment using HAQ and SF-36.¹¹⁷

PROGNOSIS DETERMINATION

A great progress has been made in identifying the clinical and laboratory characteristics associated with greater joint destruction and worse prognosis. These characteristics include female sex; smoking; disease onset at an earlier age; low socioeconomic level; presence of high titers of autoantibodies, such as RF and anti-CCP; persistently high ESR and CRP; large number of swollen joints; presence of extra-articular manifestations; high indices of inflammatory disease activity, such as DAS and its variations, SDAI or CDAI; and presence of early erosions (Table 8).¹¹⁸⁻¹²⁸

Table 8
Characteristics associated with a greater radiographic progression and worse prognosis in patients with rheumatoid arthritis

Female
Smoking
Low socioeconomic level
Disease onset at an earlier age
High titers of rheumatoid factor and/or anti-CCP
Persistently high acute-phase reactants (erythrocyte sedimentation rate and/or C-reactive protein)
Large number of swollen joints
Presence of extra-articular manifestations
High disease activity measured by objective disease activity indices, such as DAS28 and its variations, CDAI, and SDAI
Erosions present at an early phase of disease
Shared epitope

Anti-CCP: Anti-Cyclic Citrullinated Peptide antibodies; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score (28 joints).

Another factor associated with worse prognosis is the presence of shared epitope, but its use is limited because it is not commercially available.^{129,130}

Guidelines of the Brazilian Society of Rheumatology for diagnosis and early assessment of rheumatoid arthritis

Based on the previous considerations and on peculiar aspects of the Brazilian socioeconomic reality, the experts of the

Table 9

Recommendations of the Brazilian Society of Rheumatology for diagnosis and early assessment of rheumatoid arthritis

Recommendation 1: The diagnosis of RA should be established considering the clinical findings and complementary test results. No isolated test, either laboratory, imaging, or histopathological, confirms the diagnosis.

Recommendation 2: Special attention should be given to differential diagnosis of arthritis, considering other causes, such as infections, spondyloarthritis, other systemic rheumatic diseases, microcrystal arthritides, endocrine disorders, and neoplastic diseases.

Recommendation 3: The rheumatoid factor is an important diagnostic test, but has limited sensitivity and specificity, mainly in early rheumatoid arthritis. Out of proper clinical context, a positive exam does not confirm the diagnosis, and a negative exam does not exclude it.

Recommendation 4: Anti-CCP is a marker with sensitivity similar to that of the rheumatoid factor, but with higher specificity, mainly in the initial phase of disease. It should be searched in patients suspected of having rheumatoid arthritis and negative rheumatoid factor.

Recommendation 5: Although unspecific, acute-phase reactants (erythrocyte sedimentation rate and/or quantitative C-reactive protein) should be measured in patients suspected of having rheumatoid arthritis.

Recommendation 6: Conventional radiography should be performed for diagnostic and prognostic assessment of disease. When necessary and available, ultrasound and magnetic resonance may be used.

Recommendation 7: Rheumatoid arthritis classification criteria (ACR/EULAR 2010), although not yet validated, may be used as a guide to aid in diagnosing patients with early RA.

Recommendation 8: One of the combined disease activity indices (DAS28, SDAI, and CDAI) should be used to assess disease activity.

Recommendation 9: At least one of the functional capacity assessment instruments, such as mHAQ or HAQ-DI, should be regularly used.

Recommendation 10: At the early assessment of disease, the presence of worse prognostic factors, such as polyarticular involvement, high titers of rheumatoid factor and/or anti-CCP, smoking, and early joint erosion, should be investigated.

Anti-CCP: Anti-Cyclic Citrullinated Peptide antibodies; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score (28 joints); mHAQ: Modified Health Assessment Questionnaire; HAQ-DI: Health Assessment Questionnaire – Disability Index.

Rheumatoid Arthritis Committee of the Brazilian Society of Rheumatology have issued the guidelines summarized in Table 9 for diagnosis and early assessment of patients with a possible diagnosis of RA.

CONCLUSIONS

This consensus was elaborated by the Rheumatoid Arthritis Committee of the Brazilian Society of Rheumatology aiming at providing guidelines for diagnosis and early assessment of RA in Brazil. Because of the large dimension of the Brazilian territory and diversity between the Brazilian macroregions, peculiar characteristics regarding the differential diagnosis and access to certain technologies (laboratory or imaging techniques) may exist in different locations.

Rheumatoid arthritis should be diagnosed, mainly in its early phase.

When not diagnosed, and, consequently, not treated adequately, a patient with RA has an increased risk to progress with persistent inflammation and progressive joint destruction. The immediate involvement of rheumatologist in the assessment of a patient with arthritis is required, considering mainly his/her greater experience and acquaintance with the possible differential diagnoses and the investigation approach.

Despite the recent guidelines about RA diagnosis, the topic should be reviewed, considering the aspects of the Brazilian reality.

Thus, the final purpose in establishing guidelines for RA is to support Brazilian rheumatologists, by using evidence obtained in controlled studies, aiming at making the diagnostic approach of RA uniform within the Brazilian socioeconomic context.

Because the knowledge in this area progresses extremely rapidly, guidelines should be regularly and periodically updated.

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