Classification and clinical assessment

A. Marchesoni¹, F. Cantini²
¹U.O.C. Day Hospital di Reumatologia, Istituto Ortopedico G. Pini, Milano;
²Unità di Reumatologia, Ospedale di Prato, Prato

SUMMARY

There are at least nine classification criteria for psoriatic arthritis (PsA) that have been proposed and used in clinical studies. With the exception of the ESSG and Bennett rules, all of the other criteria sets have a good performance in identifying PsA patients. As the CASPAR criteria are based on a robust study methodology, they are considered the current reference standard. However, if there seems to be no doubt that they are very good to classify PsA patients (very high specificity), they might be not sensitive enough to diagnose patients with unknown early PsA.

The vast clinical heterogeneity of PsA makes its assessment very challenging. Peripheral joint involvement is measured by 78/76 joint counts, spine involvement by the instruments used for ankylosing spondylitis (AS), dactylitis by involved digit count or by the Leeds dactylitis index, enthesitis by the number of affected entheses (several indices available) and psoriasis by the Psoriasis Area and Severity Index (PASI). Peripheral joint damage can be assessed by a modified van der Heijde-Sharp scoring system and axial damage by the methods used for AS or by the Psoriatic Arthritis Spondylitis Radiology Index (PASRI). As in other arthritides, global evaluation of disease activity and severity by patient and physician and assessment of disability and quality of life are widely used. Finally, composite indices that capture several clinical manifestations of PsA have been proposed and a new instrument, the Psoriatic Arthritis Disease Activity Score (PASDAS), is currently being developed.

Key words: CASPAR criteria, measurement, evaluation, instrument

CLASSIFICATION

In 1973, the seminal work of Moll and Wright led to the recognition that psoriatic arthritis (PsA) is a distinct disease different from rheumatoid arthritis (RA) and ankylosing spondylitis (AS) (1). They provided the first case definition of PsA, which was the following: “current psoriasis, history of psoriasis, or nail disease, and inflammatory joint disease, clinical sacroiliitis or inflammatory spinal disease and rheumatoid factor usually absent”. This definition underlined that in PsA both peripheral and axial joints may be involved and that rheumatoid factor should be absent. The heterogeneity of the clinical manifestations of PsA was well understood by these two Authors who proposed the following disease subgroups:
1. symmetric polyarthritis resembling RA;
2. oligoarthritis;
3. arthritis mutilans;
4. spinal disease;
5. distal interphalangeal predominant.

This subdivision, as well as the case definition, are still used today, but the current state-of-art of PsA allows better disease definition and classification. Although the Wright and Moll’s subset classification captures most of the clinical spectrum of PsA, for diagnostic and therapeutic purposes it seems more practical to rely on the fact that PsA, as one of the spondyloarthritides (SpA), may have three main patterns of presentation: synovitis of the peripheral joints, spondylitis, and enthesitis. Overlap of these manifestations often occurs and, in addition, dactylitis and inflammatory distal interphalangeal joint involvement are typical features of PsA. Psoriasis, of course, is another peculiarity of PsA, and because of the association between skin and articular involvement, the term of Psoriatic Disease has been suggested, in order to have a unifying concept of a disorder that can affect several different compartments in the same patient (2).

Since the first Moll and Wright’s case definition of PsA, the peculiar heterogeneity
of this rheumatic condition has prompted many rheumatologists with an interest in the field to propose classification criteria. Including Moll and Wright’s, there are at least eight different methods to make a “classifying” diagnosis of PsA.

The classification criteria for PsA
The main classification criteria proposed and used in the literature are the following: Moll and Wright (1), Bennett (3), Vasey and Espinoza (4), Gladman (5), ESSG (European Spondyloarthritis Study Group) (6), McGonagle (7), Fournie (8), and CASPAR (CLASsification criteria for Psoriatic ARthritis) (9). The ESSG criteria were not specifically designed for PsA but to diagnose any spondyloarthritis (SpA).

A comprehensive review of the performance of the first seven criteria sets in distinguishing between RA and PsA has been performed by Taylor W. and others a few years ago (10). As Bennet and McGonagle original criteria are impractical for clinical use, because they require synovial membrane biopsy and magnetic resonance (MR), respectively, in the Taylor’s study a modified version of these criteria was evaluated.

The main differences of the seven criteria sets are in rheumatoid factor negativity (not needed only for the Gladman and ESSG criteria), inclusion of enthesitis (only in Fournie and McGonagle criteria), the inclusion of dactylitis (Bennett, Vasey and Espinoza, Fournie, and McGonagle criteria), necessity of radiography (Bennett, Vasey and Espinoza, Fournie, and McGonagle criteria), and personal psoriasis not mandatory (ESSG, Fournie, and McGonagle criteria).

Vasey and Espinoza’s criteria (Table I) proved to be the most sensitive (99%) and specific (99%). Moll and Wright, Gladman, Fournie, and McGonagle criteria all showed a good performance (sensitivity between 94% and 99% and specificity between 88% and 99%), but the Fournie’s were not applicable in about 25% of the PsA patients (because they require HLA analysis). Both Bennett and ESSG criteria showed a low sensitivity (0.69% and 0.56%, respectively). Similar results were found in the CASPAR study, where all the seven criteria sets were applied to the patient cohort used for the study (9).

In summary, with the exception of the ESSG and Bennett rules, all of the other old criteria sets have a good performance in distinguishing PsA and RA patients. However, Fournie’s rule is not applicable in about 25% of case and McGonagle’s is useful only in an amended version. As the Vasey and Espinoza’s rule has the highest sensitivity and specificity, it may be used as the standard reference of the old criteria sets.

The main limitation of all these criteria is that they were not derived from observed data (with the exception of the ESSG criteria) and that they were never validated. In addition, the very existence of several equivalent criteria sets is by itself a drawback, being a source of confusion when classification criteria for inclusion into clinical and laboratory studies are needed.

These limitations prompted a study whose target was to create a new rule based on observed data and solid methodology.

Table I - Vasey and Espinoza criteria.

<table>
<thead>
<tr>
<th>Psoriatic skin or nail involvement (current psoriasis, history of psoriasis, or nail disease)</th>
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<tbody>
<tr>
<td>(a) Peripheral pattern (any of):</td>
<td>1/ DIP involvement (finger DIP swollen)</td>
</tr>
<tr>
<td></td>
<td>2/ Asymmetry or dactylitis</td>
</tr>
<tr>
<td></td>
<td>3/ Symmetry in absence of RF and nodules</td>
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<tr>
<td></td>
<td>4/ Pencil-in-cup deformity, whittling of terminal phalanges, fluffy periostitis and bony ankylosis (radiographic osteolysis, tuft erosion, ankylosis, or juxta-articular new bone formation)</td>
</tr>
<tr>
<td>(b) Axial pattern (any of):</td>
<td>1/ Spinal pain and stiffness with the restriction of motion present for over 4 weeks</td>
</tr>
<tr>
<td></td>
<td>2/ Grade 2 symmetric sacroiliitis according to the New York criteria</td>
</tr>
<tr>
<td></td>
<td>3/ Grade 3 or 4 unilateral sacroiliitis</td>
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</tbody>
</table>
The CASPAR criteria
The CASPAR study (9) involved 30 rheumatology clinics in 13 countries. The diagnosis was based upon opinions of rheumatologist with longstanding expertise in PsA. Data were collected on 588 PsA patients and 536 control cases, matched for age and disease duration, with other inflammatory arthropaties, mostly RA (71.6%). All of the standard clinical, laboratory and radiographic features were collected and compared using univariate analysis and two different multivariate models. The following clinical and radiographic features proved to be >90% specific for PsA: psoriasis (current or in the past), psoriasis in the family, nail distrophy, enthesitis, dactylitis, distal interphalangeal joint involvement, uveitis, virtually all of the spine radiographic changes typical of the axial SpAs, unilateral sacroiliitis, iuxta-articular new bone formation, interphalangeal bony ankylosis, and tuft osteolysis.

However, most of these features were poorly sensitive and, eventually, only five features were independently predictive of PsA as opposed to other inflammatory arthropaties: psoriasis (current, or a history of, or in the family), nail distrophy, dactylitis (current or a history of), absence of rheumatoid factor, and iuxta-articular new bone formation, interphalangeal bony ankylosis, and tuft osteolysis. Interestingly enough, anti-cyclic citrullinated peptide antibodies, which are highly specific for RA, could not discriminate the two patient group due to a relatively low frequency in the control cases. A Receiver Operator Characteristic (ROC) curve derived using the number of the distinguishing features of each individual PsA patient (area under the curve 0.989, 95% CI 0.984-0.995) revealed the best sensitivity (91.4%) and specificity (98.7%) was reached with three or more items. The CASPAR criteria (Table II) were then identified as the presence of three or more features in a person with peripheral arthritis or spondylitis or enthesitis. Current psoriasis by itself was scored two points because of its weight in the individual patient. In the subjects classified by both Vasey and Espinoza and CASPAR methods (n=1,095), the sensitivities were 0.972 and 0.914, respectively, and the specificities were 0.960 and 0.987, respectively.

The CASPAR study has a number of strength. The accuracy of the diagnostic gold standard was confirmed by a statistic defined gold standard obtained using the “Latent Class Analysis” technique, the diagnostic bias was reduced by the high number of involved Centres, the large number of cases and controls allowed for small statistical differences, the high number of examined items should reduce the issues of circularity, and the multivariate results were supported by a robust statistical analysis. The CASPAR method

| Table II - The CASPAR criteria. |
|---------------------------------|---------------------------------|
| **Established inflammatory skeletal disease (joint, spine, or enthesal)** | With 3 or more points (score 2) |
| 1. Psoriasis (one of a, b, c)   | (a) Current psoriasis*          |
|                                 | Psoriatic skin or scalp disease present today as judged by a rheumatologist or dermatologist |
|                                 | (b) Personal history of psoriasis |
|                                 | A history of psoriasis that may be obtained from patient, family doctor, dermatologist or rheumatologist |
|                                 | (c) Family history of psoriasis |
|                                 | A history of psoriasis in a first or second degree relative according to patient report |
| 2. Psoriatic nail dystrophy     |                                  |
|                                 | Typical psoriatic nail dystrophy including onycholysis, pitting and hyperkeratosis observed on current physical examination |
| 3. A negative test for rheumatoid factor | By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range |
| 4. Dactylitis (one of a, b)     | (a) Current dactylitis          |
|                                 | Swelling of an entire digit     |
|                                 | (b) History of dactylitis       |
|                                 | A history of dactylitis recorded by a rheumatologist |
| 5. Radiological evidence of juxta-articular new bone formation | Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain x-rays of hand or foot |
is simple and can be easily used in daily clinical practice. It was a bit less sensitive than the Vasey and Espinoza’s rule but it showed the best specificity, making it the most suitable to classify patients for clinical and scientific research.

As the CASPAR study was performed in patients with known and well-established diseases, its results do not necessarily apply to early-onset cases and to the general population.

In a specific study in patients with early PsA, the CASPAR criteria showed a relatively slow sensitivity (73.3%) (11) and in a study on the prevalence of rheumatic conditions in patients with psoriasis attending a tertiary dermatologic clinic, the Vasey and Espinoza rule performed better than the CASPAR method (sensitivity 99.1% and 90%, respectively) (12). Therefore, if there seems to be no doubt that the CASPAR criteria are very good to classify PsA patients (very high specificity), they should be used with caution in diagnosing patients with unknown early arthritis.

As in the CASPAR study the presence of inflammatory arthritis was required as inclusion criterion, the available data could not be used to provide an operational definition of inflammatory arthritic disease. A precise definition of “inflammatory skeletal involvement” should be formulated and then validated by a specific study. This should help rheumatologists to use the CASPAR criteria as a diagnostic tool. Finally, as the radiographic criterion only applies to late disease and it is not always available in day-to-day practice, its modification should further enhance the diagnostic performance of this method.

### CLINICAL ASSESSMENT

PsA is a composite inflammatory disorder and the measures to assess its activity and response to therapy should include the evaluation of peripheral arthritis, axial involvement, enthesitis, dactylitis, and psoriasis. Assessment of PsA has generally been accomplished by adapting measures used in clinical trials for RA, psoriasis and, to a lesser extent, AS. Table III summarizes the measures to assess all of the previously mentioned clinical variables in PsA patients.

**Table III - Measures to assess disease activity and response to therapy in patients with PsA.**

<table>
<thead>
<tr>
<th>Domains</th>
<th>Instruments</th>
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<tbody>
<tr>
<td>Joint assessment</td>
<td>68/66 Tender/Swollen joint count, ACR, DAS28, PsArC</td>
</tr>
<tr>
<td>Axial assessment</td>
<td>BASDAI, BASFI, BASMI</td>
</tr>
<tr>
<td>Fatigue</td>
<td>FACIT, MFI, VAS</td>
</tr>
<tr>
<td>Pain</td>
<td>VAS</td>
</tr>
<tr>
<td>PGA</td>
<td>VAS (global, skin and joints)</td>
</tr>
<tr>
<td>PhGA</td>
<td>VAS (global, skin and joints)</td>
</tr>
<tr>
<td>Function/QOL</td>
<td>HAQ, SF-36, PsAQoL, DLQI</td>
</tr>
<tr>
<td>Enthesitis assessment</td>
<td>Mander’s index, MASES, SPARCC</td>
</tr>
<tr>
<td>Dactylitis assessment</td>
<td>Leeds index, present/absent, acute/chronic</td>
</tr>
<tr>
<td>Laboratory</td>
<td>ESR, CRP</td>
</tr>
<tr>
<td>Imaging</td>
<td>Radiography (modified Sharp or van der Heijde-Sharp, BASRI, mSASSS, Psari), MRI, US</td>
</tr>
<tr>
<td>Skin disease</td>
<td>PASI, Target lesion</td>
</tr>
</tbody>
</table>

Abbreviations. ACR = American College of Rheumatology; DAS = disease activity state; PsARC = Psoriatic Arthritis Response Criteria measure; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BASFI = Bath ankylosing spondylitis functional index; BASMI = Bath Ankylosing Spondylitis Metrology Index; FACIT = Functional Assessment of Chronic Illness Therapy measurement; MFI = Multidimensional Fatigue Inventory; VAS = visual analog scale; PGA = Patient Global Assessment; PhGA = Physician Global Assessment; HAQ = Health Assessment Questionnaire; SF-36: Short Form-36; PsAQoL = Psoriatic Arthritis Quality of Life questionnaire; DLQI = Dermatology Life Quality; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; SPARCC = Spondyloarthritis Research Consortium of Canada index; ESR = Erythrocyte Sedimentation Rate; BASRI=Bath AS Radiology Index; mSASSS = modified Stoke AS Spine Score; PASRI = Psoriatic Arthritis Spondylitis Index; CRP = C-Reactive Protein; MRI= Magnetic Resonance Imaging; US = Ultrasound; PASI = Psoriasis Area Severity Index.
**Joint assessment**

ACR response criteria using 68/66 tender/swollen joint count have been recommended for articular evaluation in PsA at OMERACT 8 (13). This measure is useful to reliably assess disease activity in PsA characterized by predominant peripheral joint involvement. However, in the first published study of a biological agent in the treatment of PsA (14), the Psoriatic Arthritis Response Criteria (PsARC), as originally proposed by Clegg et al. (15), was used as primary outcome measure. It includes a modified version of the ACR joint count by adding the evaluation of the distal interphalangeal joints of the feet and carpometacarpal joints of the hands to yield a 78 and 76 joint count. PsARC score is also composed by the Patient Global Assessment (graded 0 to 5) and Physician Global Assessment (graded 0 to 5). PsARC requires improvement in at least two items with no worsening of any of them, improvement in joint counts defined as decrease by ≥30% and improvement in global assessment ≥1. Even if the most widely used measure of drug efficacy is the ACR response criteria scoring system, PsARC is the only outcome measure specifically designed for PsA and it has been used in several trial of traditional DMARDs and biologics in PsA.

Recently, a statistical model of PsA assessment, the PsAJAI (PsA Joint Activity Index) has been developed and recommended for clinical trials (16). It is based on a weighted sum of 30% improvement in core measures with weights of two given to the joint count measure, the C-reactive protein laboratory measure, and the physician global assessment of disease activity measure.

Weights of 1 should be given to the remaining 30% improvement measures including pain, patient global assessment of disease activity, and the Health Assessment Questionnaire.

Although the DAS28 has been used in several trials of biologics (17), this scoring system does not include the evaluation of distal inter-phalangeal and feet joints and it does not seem adequate for PsA.

**Axial assessment**

The assessment of spine involvement in PsA is mainly based upon the scoring systems currently used for AS: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) (18), BASFI (Bath Ankylosing Spondylitis Functional Index) (19), BASMI (Bath Ankylosing Spondylitis Metrology Index) (20), and ASAS response criteria (21).

The BASDAI is a self-administered instrument for assessing disease activity. This index consists of six questions answered on a 10-cm horizontal visual analog scale (VAS) that records the patient’s assessment severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness (both qualitative and quantitative). In addition to being reliable, sensitive to change, and reflective of the entire spectrum of disease, it is readily understood by patients and it only takes a few minutes to be completed. The BASFI consists of 10 specific questions regarding the ability of AS patients to perform specific common functions. In addition, there are 2 questions regarding the ability of the patient to cope with everyday life. Each question is answered on a 10-cm horizontal visual analog scale, the mean of which gives the BASFI score. The BASFI is simple, reliable, and sensitive to change across the spectrum of disease. The BASMI includes five clinical measures: tragus-to-wall distance, lumbar flexion, measured by the Schober’s test (22), cervical rotation, measured by the ability of the patient to rotate the neck from side to side, lumbar-side flexion, measured as the difference between the distance from the third finger and the floor when the patient stands straight and when the patient bends sideways with the knees straight, and intermalleolar distance, measured as the distance between the two malleoli when the patient lies down with the hips fully abducted. The ASAS response criteria incorporate four domains: physical function, pain, patient global assessment and inflammation (mean of the two BASDAI questions on morning stiffness). An improvement of ≥20% and a net improvement of ≥10 units on a scale of 0-100 in each of
the three domains with no worsening in the fourth define the response criteria. The term ASAS 20 means an improvement of at least 20% of these core sets of criteria and allows the calculation of treatment response between the ‘responder’ and the ‘no responder’ patients. ASAS 40 and ASAS partial remission (defined as a value ≤ 20 in all four domains) can also be used.

Enthesitis assessment

As shown in table IV, different methods of assessment of enthesitis were developed and validated in patients with AS. Although currently applied to PsA patients, it should be noted that only the Leeds enthesitis index has been designed for PsA.

Dactylitis assessment

Dactylitis is commonly assessed as number of affected digits. Recently, a simplified dactylitis index, the Leeds dactylitis index (LDI) (28) has been proposed and adopted for clinical trial by OMERACT (29). The LDI items are summarized below:

1. measures the ratio of the circumference of the affected digit to the circumference of the digit on the opposite hand or foot: a minimum difference of 10% is used to define a dactylitic digit;
2. if ipsilateral and controlateral digits are involved a table of normative values is used to provide the comparison;
3. assessment of the degree of tenderness of dactylitis using the Ritchie grading index. A 0 to 1 scale is used in response to a squeeze from the examiner’s hand: 0= non tender, 1= tender;
4. perform the following calculation for each involved digit: (circumference of the affected digit/circumference of the digit on the opposite side) X (Ritchie degree of tenderness);
5. add score to give the grand total.

Fatigue

There are several measures of fatigue, including a visual analogue scale, the Krupp Fatigue Severity Scale (FSS) (30), and recently reported elaborate measures of fatigue such as the Functional Assessment of Chronic Illness Therapy (FACIT) (31) and Multidimensional Fatigue Inventory (MFI) (32). Of these, only the Krupp FSS has
been studied in PsA with good correlation with actively inflamed joints (33).

**Patient global assessment (PGA) and physician global assessment (PhGA)**
The global, skin and joint PsA activity is evaluated independently by the patient and physician through a visual analogue scale 0 to 100 mm. A recent study suggested that joint and skin activity can be reliably assessed by the patients on a single VAS (34).

**Function/quality of life (QOL)**
The loss of function and quality of life in PsA is usually evaluated through several questionnaires including the Health Assessment Questionnaire Disability Index (HAQ), the Short Form-36 (SF-36), the Psoriatic Arthritis Quality of Life questionnaire (PsAQoL), and the Dermatology Life Quality (DLQI). The HAQ Disability Index is a simple two-page survey that assesses the patient’s ability to perform eight activities of daily living including dressing, arising, eating and walking, reaching and grasping, maintaining hygiene, and maintaining daily activity. The SF-36 is the best-known questionnaire among experts in measuring health status and it has been validated in PsA (35). SF-36 has been used in over 2,000 published research studies and it assesses 8 domains of health status including physical functioning, pain, vitality, social functioning, psychological functioning, general health perceptions, and role limitations due to physical and emotional problems.

**Laboratory**
Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are currently employed in clinical trials and real-life practice to evaluate the disease activity in PsA patients. However, these parameters are not good indicators of disease activity and ESR is elevated in only half of the patients with PsA (36).

**Imaging**
Peripheral joint damage is evaluated by the modified Sharp score (37). This method include the radiological evaluation for erosion and joint space narrowing of 16 and 15 areas of the hands, respectively, all the metatarso-phalangeal joints, and the interphalangeal joints of the first toes.

Magnetic resonance imaging (MRI) and Ultrasound (US) have been increasingly reported as accurate methods for the detection of articular erosions, synovitis, enthesitis and dactylitis. However, the potential role of US and MRI for use in clinical practice and research has not been definitively assessed by OMERACT (38).

It has been shown that radiographic axial involvement can be assessed by two instruments used for AS: the Bath AS Radiology Index (BASRI) and the modified Stoke AS Spine Score (mSASSS) (39). In addition, a specific tool for psoriatic axial involvement, the Psoriatic Arthritis Spondylitis Radiology Index (PASRI), has been recently proposed (40).

MRI scoring systems for sacroiliitis and spondylitis have been suggested for AS but have not been tested in PsA.

**Skin disease**
The Psoriasis Area Severity Index (PASI) has been employed in all clinical trials of PsA and is the widely used in clinical practice. It encompasses the degree of erythema, induration, and scale, as well as the area involved, in the head, trunk, and upper and lower extremity. The severity of each of these items is graded and the sum constitutes the PASI score.

**Clinical remission assessment/composite indices**
No remission criteria have been standardized for PsA. Ideally, remission should be identified by an index capable of evaluating all of the different clinical manifestations of PsA and should meet the three requirements of the OMERACT filter (truth, discrimination, and feasibility). In a recent Italian study (41) remission in peripheral PsA was defined by fatigue (VAS 1–100 mm) <10, pain (VAS 1-100 mm) <10, articular morning stiffness <15 minutes, active (tender and swollen) joint count 0, normal ESR and CRP values, and absence of dactylitis, enthesitis, tenosynovitis, in-
flammatotory spinal pain, and extra-articular manifestations. Coates et al. suggested that a PsA patient could be classified as achieving minimal disease activity when meeting five of seven following criteria: tender joint count ≤1, swollen joint count ≤1, PASI ≤1, patient global disease activity (on VAS) ≤20, HAQ ≤0.5, tender enthesal points ≤1 (42). The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) developed the Composite Psoriatic Disease Activity Index (CPDAI), which assesses disease activity in five domains: skin, joints, entheses, dactylitis and spine (43). The Vienna group adopted the Disease Activity in REActive arthritis (DAREA) (44) composite measure and re-introduced it as Disease Activity in PSoriatic Arthritis (DAPSA) (45), which only assess peripheral joint disease activity. Finally, a new specific instrument, the psoriatic arthritis disease activity score (PASDAS), is being developed from the data of an international multicentre study promoted by GRAPPA.

REFERENCES

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