

Psoriatic Arthritis Mutilans: Clinical and Radiographic Criteria. A Systematic Review

Amir Haddad, Sindhu R. Johnson, Mansour Somaily, Rouhi Fazelzad, Amie T. Kron, Cathy Chau, and Vinod Chandran

ABSTRACT. Objective. Research on psoriatic arthritis mutilans (PAM), the most severe form of psoriatic arthritis, is impeded by the lack of an accepted classification criteria. We performed a systematic review of the literature to identify and synthesize clinical and radiographic features associated with the definition of PAM.

Methods. A systematic literature search limited to human studies was conducted without language restriction. Abstracts were independently screened by 2 investigators and studies that reported information on patients with PAM were included. A standardized form was used to independently collect clinical and radiographic items defining PAM, patient's demographics, disease characteristics, and outcomes.

Results. There were 8570 citations searched to identify 112 articles for full review and 58 articles for data abstraction. We identified 8 definitions of PAM that were used in 283 subjects with a mean age \pm SD at diagnosis of PsA of 33.9 ± 8.2 years. Disease manifestations (prevalence) included dactylitis (29–64%), enthesitis (29–32%), axial disease (14–27%), and nail lesions (47%). PAM definitions include 1 (n = 2 studies) or more (n = 14 studies) joints involving interphalangeal, metacarpophalangeal, or metatarsophalangeal joints. The most prevalent PAM clinical features were digital telescoping (34%), digital shortening (33%), and flail joints (22%). The most prevalent PAM radiographic items were bone resorption (41%), pencil-in-cup change (16%), total joint erosions (14%), ankylosis (21%), and subluxation (7%).

Conclusion. We have identified 8 definitions of PAM, and synthesized the clinical and radiographic items that are important for the classification of PAM. We have established the groundwork for future development classification criteria for PAM. (J Rheumatol First Release June 15 2015; doi:10.3899/jrheum.141545)

Keyword Indexing Terms:

PSORIASIS
ANKYLOSIS

SPONDYLOARTHRITIS

OSTEOLYSIS
CLASSIFICATION CRITERIA

From the University of Toronto Psoriatic Arthritis Clinic, and Division of Rheumatology, Toronto Western Hospital; Institute of Health Policy, Management and Evaluation, and Division of Rheumatology, Department of Medicine, University of Toronto; University Health Network, Toronto, Ontario, Canada.

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A. Haddad, MD, University of Toronto Psoriatic Arthritis Clinic, Toronto Western Hospital; S.R. Johnson, MD, PhD, Division of Rheumatology, Toronto Western Hospital, and Institute of Health Policy, Management and Evaluation, and Division of Rheumatology, Department of Medicine, University of Toronto; M. Somaily, MD, University of Toronto Psoriatic Arthritis Clinic, Toronto Western Hospital; R. Fazelzad, BSc, MSc, University Health Network; A.T. Kron, BSc (Honors); C. Chau, BMath, CIM, Division of Rheumatology, Toronto Western Hospital; V. Chandran, MBBS, MD, DM, PhD, University of Toronto Psoriatic Arthritis Clinic, and Division of Rheumatology, Toronto Western Hospital, and Division of Rheumatology, Department of Medicine, University of Toronto.

Address correspondence to Dr. V. Chandran, 1E 416, Toronto Western Hospital, 399 Bathurst St., Toronto, Ontario M5T 2S8, Canada.
E-mail: vchandra@uhnresearch.ca

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Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease associated with psoriasis¹. Moll and Wright were the first to define PsA as “psoriasis associated with inflammatory arthritis (peripheral arthritis and/or spondylitis) and usually a negative serologic test for rheumatoid factor”². Because of the phenotypic variability of the clinical presentations of PsA, they suggested that PsA could be classified into 5 predominant patterns: asymmetric oligoarthritis, symmetric polyarthritis similar to rheumatoid arthritis, spondylitis, distal interphalangeal joint arthritis, and arthritis mutilans². PsA mutilans (PAM) is considered the most severe form of PsA, affecting about 5% of patients². Although the occurrence of arthritis mutilans associated with PsA is often described as a relatively rare event, studies have reported a wide prevalence of 2–21%, mainly because of differences in the definition used by investigators³.

Affected patients experience severe joint destruction and functional disability. It is therefore important that we identify clinical predictors and biomarkers for PAM so that patients at risk are identified early, and appropriate therapeutic inter-

ventions are instituted to prevent joint destruction and loss of function and to preserve quality of life⁴. However, studies aiming to identify clinical predictors or biomarkers for PAM have been impeded by the lack of consensus on the definition³. The Group of Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) is now aiming to develop a consensus definition of PAM⁵.

Concurrently, it has been recognized that in the absence of a single diagnostic test, rheumatic diseases with a variety of manifestations would benefit from classification criteria. Classification criteria facilitate the inclusion of more homogeneous groups of patients into clinical trials and facilitate more even comparisons across studies. There have been recommendations for increased methodological rigor in classification criteria development and advanced methodology resulting in a new era of classification criteria^{6,7,8,9,10,11,12,13}. As the first phase of PAM classification criteria development, we performed a systematic review of the literature to identify and synthesize the clinical and radiographic criteria that are used to characterize PAM.

MATERIALS AND METHODS

Data sources. A systematic search of the published literature was conducted using Medline (1946–October 2013), Embase (1974–October 2013), Cochrane Central Register for Controlled trials (1993–2013), Cochrane databases of Systematic Reviews (2005–October 2013), and Cumulative Index to Nursing and Allied Health Literature, 1984–2013 (CINAHL) by an information specialist through the University Health Network library services (RF) without language restriction, but limited to human studies.

Search terms. The keyword terms used in the search of each database are outlined in Appendix 1 (available online at jrheum.org).

Search strategy. A protocol was developed and a systematic review performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement¹⁴. Two investigators (AH, MS) independently screened titles and abstracts and included studies that had reported patients with PsA and arthritis mutilans. The selected articles were retrieved for extraction of the data with source de-identification. Machine translation software was used to translate articles to English. The bibliography of the eligible articles was searched and eligible studies were included for data extraction. Two investigators independently used a standardized form (Appendix 2, available online at jrheum.org) to collect items used in the definition of PAM, including the presence of shortening of digits, digital telescoping, flail joints, number and type of joints affected, time to joint destruction, the presence of total erosions at both sides of the joint, bone resorption, pencil-in-cup change, ankylosis, and subluxation. These are illustrated in Figure 1. The demographics, disease characteristics, and clinical and radiographic outcomes of study subjects were recorded. Discrepancies were resolved by consensus or involving a third investigator (VC).

Citation index. Many sets of criteria have been proposed for PAM. We were interested in evaluating those that were commonly used to classify patients with disease. Web of Science (version 5.13.1, Thomson Scientific) was used to search the Science Citation Index Expanded (1945–2013) to identify the number of times each article was cited. This approach has been used to evaluate classification criteria for other rheumatic diseases^{15,16}.

Analysis. Descriptive statistics were used to aggregate the data without weighting. If the clinical and radiographic features were mentioned in the definition, they would be marked as present; the sum of the total studies reporting the specific items was divided by the total studies reported to calculate the proportion.



Figure 1. Illustration of radiographic features of PAM. Presence of total erosion at both sides of the joint (marked as TJD). Bone resorption involving of the epiphyseal head (marked as E). Bone resorption extending to the diaphysis (marked as D). Presence of bone whittling, resorption of bone causing pinpoint end (marked as W). Presence of pencil-in-cup change, resorption of bone causing cupping of distal or proximal end of the bone with whittling of the opposite side (marked as C). Presence of ankylosis (marked as A). PAM: psoriatic arthritis mutilans.

RESULTS

Literature search. There were 8570 citations identified (Figure 2). Citations were excluded if they were not related to the topic ($n = 7375$), reported patients with other rheumatic diseases ($n = 47$), did not report PAM as an outcome ($n = 53$), or were duplicate citations ($n = 983$). Of the 112 articles selected for full review, 58 were eligible for data abstraction^{2,17–27,28–38,39–49,50–60,61–71,72,73}. These included 5 additional papers that were not identified in the computerized search^{69,70,71,72,73}. The computerized search was limited to publications after 1946 (the inception date of the Medline database) and were found when the bibliography of the eligible studies was searched. Of the total 58 studies that were included for data abstraction, there were 17 review articles, 22 case studies, 14 cohort studies, 6 case series, 2 case-control studies, and 2 cross-sectional studies. We had a 95% agreement in inclusion of the papers and 90% agreement in data abstraction between 2 independent reviews, and all discrepancies were resolved by consensus. Because of the heterogeneity across studies and the descriptive nature of the findings, a metaanalysis was not performed.

Demographics and disease characteristics of subjects with PAM. Demographic and disease characteristics were reported in 45 studies (78%) that included a total of 283 subjects^{17,18,20,21,22,23,24,26,27,28,29,30,33,34,36,37,39,40,42,44,45,47,48,49,50,51,52,53,54,56,59–69,70,71,72,73}. Based on reported data, 86/166

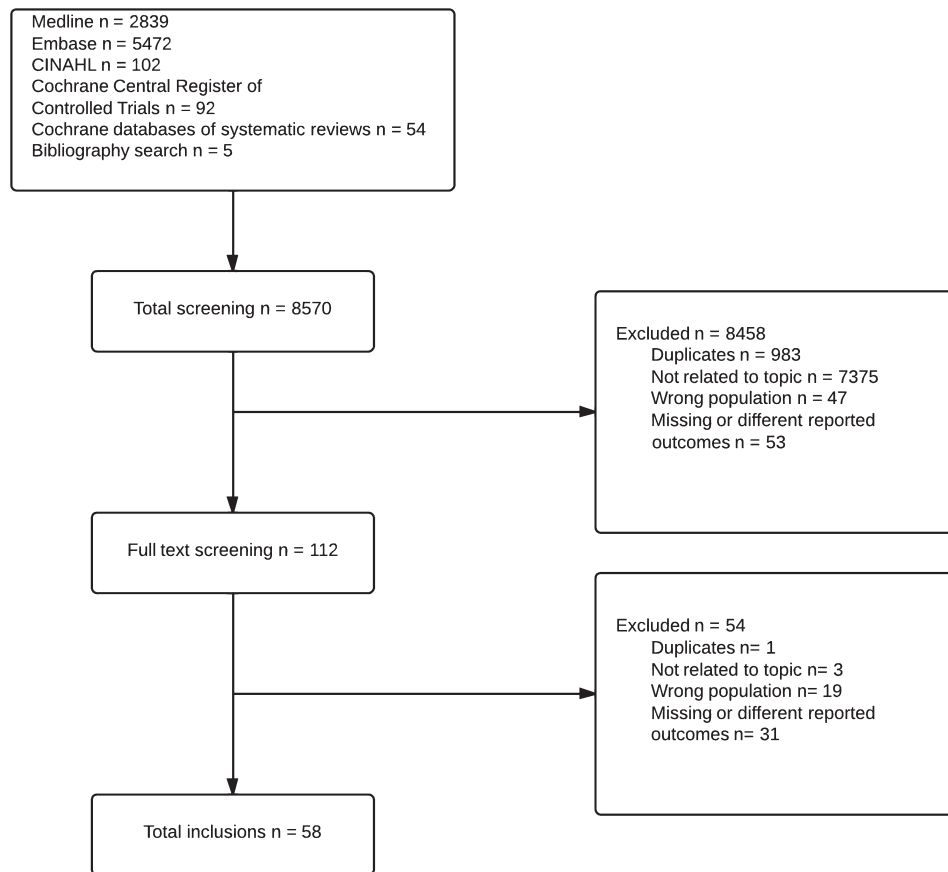


Figure 2. Flow diagram of search results. CINAHL: Cumulative Index to Nursing and Allied Health Literature, 1984–2013.

(51.6%) of the study subjects were men (sex was reported in 59% of the study population) and had a mean age (SD) of 54.1 years (7.3; reported in 52% of cases). Most of the patients had psoriasis before the diagnosis of PsA, with a mean age at diagnosis of psoriasis of 28.7 years (7.4; reported on 49% of cases) and PsA of 33.9 years (8.2; reported on 57% of cases). Dactylitis was present in 29–64% of the cases, whereas enthesitis was reported to occur in 29–32%^{21,22}. Axial disease was present in 14–27% of patients with PAM^{20,21}. The presence of nail lesions was reported in 47% of patients with PAM in 1 case series²¹. Patients with PAM had 1^{33,37} or more^{22,24,25,28,34,40,45,47,52,56,60,63,67,69} affected joints involving any of the interphalangeal, metacarpophalangeal, or metatarsophalangeal joints. PAM was reported to occur within a few months^{25,37} and up to several years^{33,45} after PsA onset.

Definitions of PAM. Eight definitions for PAM have been proposed in the literature and are summarized in Table 1. Prior to 1973, there were case reports or case series on patients with arthritis mutilans in the presence^{69,70,71,72,73} or absence^{75,76} of psoriasis. All patients had articular manifestations with severe joint destruction and either digital tapering (opera glass hands) or joint ankylosis. The most commonly

cited definition for PAM reported in 50% of the studies (n = 29) was the definition by Moll and Wright, which described “patients with arthritis mutilans often complicated with digital telescoping or the *doigt en lorgnette* deformity resulting from severe osteolysis; these patients often have sacroiliitis”². Twenty-one percent of the studies (n = 12) did not provide a definition.

The clinical and radiographic features of PAM. The clinical features that were used in the definitions are summarized in Table 2. They included the presence of digital telescoping (n = 20, 34%), presence of digital shortening (n = 19, 33%), and flail joints (n = 13, 22%). Only 17% of the articles (n = 10) specified the type of joints affected with no consensus because some investigators generalized the definition for the small joints of hands or feet^{19,23,30,31,43,48,52,55,60} and others specified only the interphalangeal joints^{18,45}. Other studies included the metacarpophalangeal and metatarsophalangeal joints^{52,55,60}. A few papers commented on the number of joint affected^{17,21,30,31}. Helliwell, *et al*¹⁷ suggested that a presence of at least 1 affected joint is required, but PAM was characterized as a polyarticular disease in other studies^{21,30}. Four studies commented on the time to joint destruction,

Table 1. Definitions for PAM proposed in the literature.

Study	Definition	Citation Index
Moll and Wright ²	Digital telescoping (<i>doigt en lorgnette</i>) or opera glass finger resulting from severe osteolysis.	768
McGonagle, <i>et al</i> ¹⁹	Diffuse bone destruction of the small joints of hands, especially the DIP joints, with bone changes that are reminiscent of enthesopathy-associated bone lesions.	169
Helliwell, <i>et al</i> ¹⁷	Severe destructive changes in small joints of hands and feet with telescoping of at least 1 digit.	132
Marsal, <i>et al</i> ¹⁸	Complete erosion of the metacarpal or metatarsal head and the corresponding epiphysis of the phalanx or both epiphyses of an interphalangeal joint of a finger or a toe.	75
Tan, <i>et al</i> ²⁰	Pencil-in-cup deformities or bone lysis causing 30–50% resorption of proximal and middle phalanges manifesting clinically as digital shortening or radiographically as complete erosion of bone at both sides of the joints.	11
Helliwell ²¹	Patients with PAM are more likely to have polyarticular, symmetrical disease for a long duration and positive CCP in the context of bone osteolysis, ankylosis, enthesal abnormalities, and spinal abnormalities.	4
Gudbjornsson, <i>et al</i> ²²	Presence of clinical arthritis of type PAM that is also radiographically confirmed.	1
Chandran, <i>et al</i> ⁷⁴	≥ 5 joints with grade IV damage using the modified Steinbrocker scoring method.	0

DIP: distal interphalangeal; PAM: psoriatic arthritis mutilans; CCP: cyclic citrullinated peptide antibodies.

Table 2. Clinical and radiographic features in the definition of PAM.

Criteria	Description	Studies Reporting Items, n (%)	References
Clinical	Presence of digital shortening	19 (33)	2,25,26,31,34,37,38,41,45,46, 48,51,52,54,55,57,58,59,60
	Presence of digital telescoping	20 (34)	2,17,26,30,34,37,38,41,45,46, 48,51,52,54,55,58,59,60,66
Radiographic	Presence of flail joints	13 (22)	2,26,30,37,38,41,48,51,52,54,55,58,60
	Bone resorption	24 (41)	2,18,19,21,22,25,26,30,31,34,37,38,41,43, 45,46,48,52,54,55,56,58,60,66,68
	Presence of joint ankylosis	12 (21)	2,21,30,31,45,52,55,56,58,60
	Presence of pencil-in-cup change	9 (16)	22,25,31,45,52,55,58,60,66
	Presence of total joint erosion	8 (14)	18,20,34,55,58,60,66
	Presence of joint subluxation	4 (7)	31,52,55,58

PAM: psoriatic arthritis mutilans.

describing it as a rapid process^{28,31} in patients with long disease duration^{21,26}.

The radiographic items for PAM included the presence of bone resorption (41%, n = 24), joint ankylosis (21%, n = 12), pencil-in-cup change (16%, n = 9), total joint erosions (14%, n = 8), and subluxation (7%, n = 4) as shown in Table 2.

DISCUSSION

Arthritis mutilans is recognized as the most severe destructive form of PsA. However, criteria for the classification of PAM have not yet been formulated. Patients with PAM experience severe joint destruction and functional disability. It is, therefore, crucial that we identify clinical predictors and biomarkers for PAM so that patients at risk are identified

early and appropriate therapeutic intervention instituted. Criteria for the classification of PAM will facilitate clinical and biomarker research on this severe form of PsA. Classification criteria for PAM will identify more homogeneous groups of patients for inclusion into research studies, and facilitate comparisons across studies¹⁶. Similarly, it may decrease misclassification. We, therefore, conducted a systematic search of the literature to review definitions of PAM reported previously, and synthesized the clinical and radiographic domains used to describe this extreme phenotype. Synthesis of the literature is a necessary prerequisite for modern classification criteria development¹⁶.

Our systematic review reveals 8 definitions of PAM used by investigators to date. The definition of PAM by Moll and

Wright was most commonly cited by 50% of studies, though there was variability in the clinical and radiological features used in describing the condition. Moreover, in about 21% of the studies, no definition was provided. The studies reported a wide clinical spectrum of manifestations of PAM. Clinically, at the level of the digit, the reported features most commonly included the presence of digital shortening, telescoping, and flail joints. Severe osteolysis and bone resorption were the most common radiographic characteristics used to characterize PAM. A fifth of the manuscripts included concomitant presence of joint ankylosis as a manifestation of PAM. However, joint subluxation was included as a feature in less than 10% of the articles. With regard to the number of joints involved, although PAM is generally described as polyarticular, few manuscripts have specifically mentioned the number of joints or specific joints in the definition. Thus, severe osteolysis leading to destruction of joint surfaces and proximal epiphysis manifesting as shortened, flail, or digital telescoping seems to be the most common feature used to characterize PAM. Features such as ankylosis and subluxation may be associated with PAM, but these may not be defining features. Interestingly, axial disease was reported to be present in 9 studies with varying prevalence estimates, with the highest reported prevalence being 27%^{20,21,34,36,37,39,45,49,64}.

Based on our findings, we have developed a conceptual framework for PAM and its associated clinical features as

shown in Figure 3⁷⁷. The framework emphasizes severe bone resorption (osteolysis) as the defining feature of PAM. There may be associated subluxation or ankylosis. Bone resorption leads to joint instability, resulting in the formation of flail joints. Greater degree or severity of osteolysis would lead to digital shortening and telescoping. Many of these features may be seen in the same individual, but may vary across individuals. This conceptual framework is not meant to be static, but rather to lay the groundwork for further debate and revision.

A potential limitation of this work is the influence of the definition of Moll and Wright. This phenotype relies on an older classification of PsA that was proposed in a different setting than we have today. Given this older, dominant concept of PsA, there is the threat of bias because of circularity of reasoning in the papers included in the review. Many of them rely on the initial Moll and Wright phenotype that, according to modern standards, were poorly validated in the first place. Further, we have included studies from a variety of treatment eras that may introduce confounding and calendar bias. It may be that these candidate criteria reflect established, late disease, and are insufficient in the modern treatment era. The next step may be to elicit beliefs from international PsA experts to understand what is the true “gestalt” of PAM today^{78,79}. It may be that additional candidate criteria for the various elements of the disease are needed. Indeed, we found that other potential important variables [e.g., body mass index, smoking habits, type of skin disease, HLA-B27

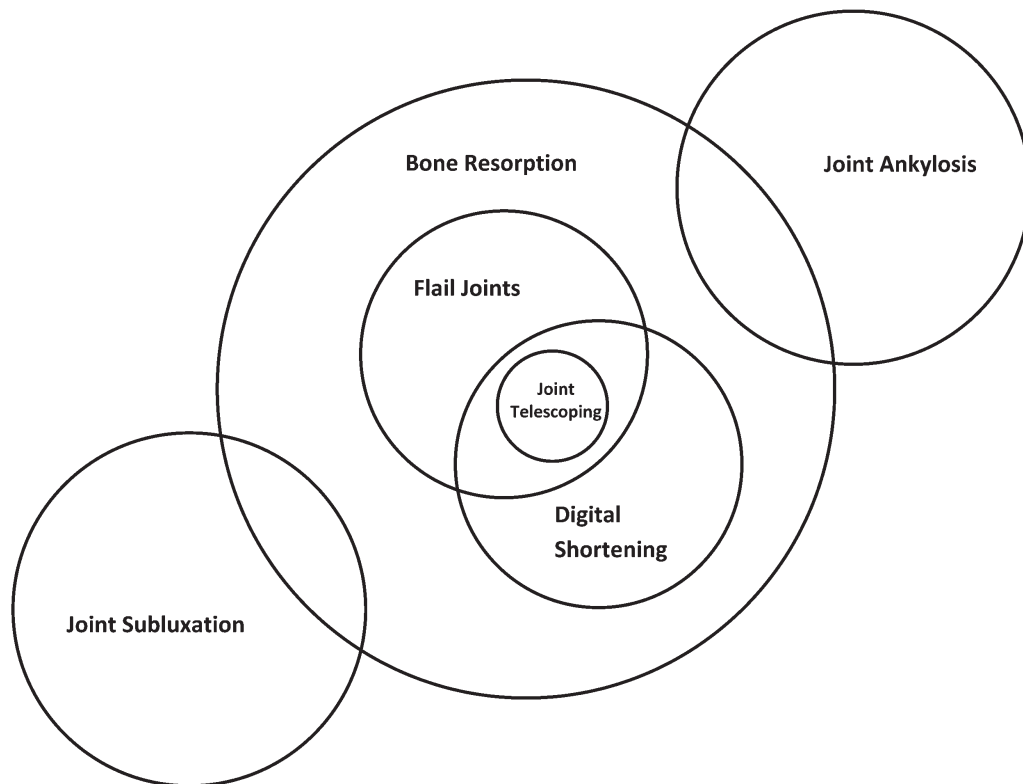


Figure 3. A conceptual framework suggesting the relationship between the clinical and radiological items of PAM, with bone resorption being a fundamental feature. PAM: psoriatic arthritis mutilans.

positivity, and autoantibodies (rheumatoid factor and anticyclic citrullinated peptide antibodies positivity)] were not well reported in the literature. Future studies should incorporate and evaluate the effect of these factors.

To our knowledge, our study is the first to systematically review the definitions used to describe PAM. We have identified key features that define this severe form of PsA, as well as features associated with the condition that, however, may not be “defining.” We have synthesized candidate criteria for consideration, and proposed a conceptual framework for debate and revision in the next phase of classification criteria development⁵. Classification criteria for PAM would facilitate research studies on identifying clinical predictors and biomarkers for PAM so that patients likely to develop PAM are identified early and longterm disability is prevented.

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The study was presented at the annual meeting of the Group for Research and Assessment of Psoriatic Arthritis in 2013 and briefly reported in the meeting report⁸⁰.

ONLINE SUPPLEMENT

Supplementary data for this article are available at jrheum.org.

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