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Plain Radiographic Instruments for Structural Damage in Peripheral Joints in Psoriatic Arthritis: A Report From the GRAPPA-OMERACT Working Group

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ABSTRACT. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)–Outcome Measures in Rheumatology (OMERACT) Psoriatic Arthritis (PsA) Core Set working group is focused on the development of a core set of instruments used to assess the domains described in the 2016 PsA Core Domain Set. At the 2021 annual meeting, the group presented an update on the domain of structural damage. In this report, we discuss the steps taken to assess the domain match and feasibility of plain radiographic instruments in the assessment of structural damage in PsA.

Key Indexing Terms: GRAPPA, outcome assessment, psoriatic arthritis

Introduction

Structural damage can be defined as abnormalities in the structure or integrity of a joint, bone, or tendon likely to be attributable to psoriatic arthritis (PsA). Structural damage is in the middle circle of the 2016 PsA Core Domain Set and should be measured at least once in the development of a new therapeutic.[1,2] It is consistently prioritized by individuals with PsA, in part due to its negative effect on physical function.[1,3,4]

Despite advances in diagnosis and therapeutics, radiographic structural damage remains common.[5,6,7,8] It is associated with disease activity and mortality, and is known to precede clinical damage.[9,10,11] There is also a discordance between disease activity

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and radiographic progression in the treatment arms of biologic randomized controlled trials (RCTs), suggesting structural damage is not a redundant outcome.[12,13,14]

In this report, we summarize progress made in advancing a radiographic instrument for the assessment of structural damage through the Outcome Measures in Rheumatology (OMERACT) Framework Instrument Selection Algorithm and report the working group's (WG) vote on the domain match and feasibility of plain radiographic instruments.

Domain Definition

The domain definition describes (1) the target population, (2) intended use for the domain (eg, clinical trials), (3) target domains (eg, joint space narrowing), (4) qualitative or literature support, and (5) sources of variability. It is modality specific, as different modalities have different sensitivities, specificities, and reliabilities for different target domains. Further, operational definitions include image acquisition variables and joint positioning, which are also modality specific.

The domain definition was drafted (AA, WT), discussed in 2 virtual WG meetings, and revised. The WG were cognizant of the importance of content-expert radiologist opinions in drafting these documents, and thus the document was subsequently reviewed by 5 expert radiologists who provided feedback by a survey (Supplementary Material 1, available with the online version of this article). A revised domain definition was next circulated to members of the WG for feedback, then finalized (Supplementary Material 2).

The target population for this domain definition was adults aged ≥ 18 years with peripheral PsA. Its intended use was for RCTs comparing a disease-modifying antirheumatic drug to a placebo or active comparator. Specifying the population and intended use ensures that when an instrument is eventually endorsed, it is used in the right population and setting.

Potential target domains were elicited from a review of the literature.[15,16] The target domains selected were joint space narrowing and joint erosion due to the frequency of these features, associations with disease activity and functional outcomes, and progression over time in RCTs (Supplementary Material 3, available with the online version of this article). Other features are uncommon and/or progress slowly when assessed by plain radiography (Supplementary Material 4). Although it is discriminative enough to warrant inclusion in the classification criteria for PsA, new bone formation including shaft or tuft periostitis and juxtaarticular osteoproliferation has not shown to progress significantly in RCTs utilizing tumor necrosis factor inhibitors up to a follow-up of 2 years.[17,18] Therefore, while it may be desirable to compare new bone formation in head-to-head trials assessing different therapeutic pathways, plain radiography may not be the appropriate modality.

The domain definition focuses on the assessment of structural damage in the hands, wrists, and feet. There is a paucity of data to support the use of plain radiography to assess structural damage in other joints in peripheral PsA. The assessment of large joints is a gap given the frequency of this phenotype; however, plain radiography may not be adequately sensitive to assess progression of structural damage in large joints in the timeframe of an RCT, and the relevant target domains may differ.

Domain Match

Candidate instruments identified from a recent literature review were assessed against the domain definition for content validity.[16] Seven instruments were included: modified Larsen, modified Steinbrocker, Ratingen score, modified total Sharp score version B (mTSS-B), modified Sharp/van der Heijde score (mSvdHs), Reductive X-Ray Score for Psoriatic Arthritis (ReXSPA), and Simplified Psoriatic Arthritis Score (SPARS).[16]

The domain match questionnaire was adapted from the OMERACT handbook and administered to participating WG members by online platform (n = 13 participants, inclusive of 1 patient research partner [PRP])[19] with reference material including radiologist feedback and a summary of the instruments (Supplementary Material 1 and Supplementary Material 5, available with the online version of this article). The results of the initial vote and available distribution data were discussed at an online WG meeting to optimize consensus. A second round of voting was undertaken (n = 14) where respondents were asked if the instrument was "Good to Go" (GREEN), "Some Cautions, but Okay" (AMBER) or "Not Right for This Application" (RED). A 50% majority response was accepted as supportive (agreement), whereas a 70% majority response was accepted as consensus. A > 15% RED response was considered a hurdle for domain match and feasibility (Supplementary Material 6).

In the final vote (Figure 1A), there was agreement from the WG that the mTSS-B and the mSvdHs had content validity (GREEN), with both target domains being assessed in the joints of the hands, wrists, and feet. This vote may reflect the recognition of instruments utilized in RCTs. There was a lack of agreement on the Ratingen score, which scores for osteoproliferation and the composite domain of destruction but not joint space narrowing. The final rating for the Ratingen was RED, given that a significant proportion of respondents (n = 6/14 [43%]) rated the instrument RED. There was consensus from the WG that the modified Larsen, modified Steinbrocker, SPARS, and ReXSPA were not appropriate for use in this setting (RED). The key WG discussion points are summarized in Table 1.

Feasibility

Feasibility was assessed among PRPs and the WG (Table 1). A live webinar followed by a Q&A session was held with PRPs. PRPs were invited to attend and/or watch a recording of the webinar at their convenience and complete a feasibility survey adapted from the OMERACT handbook with PRP input. The webinar discussed the types, importance, and effect of structural damage; the ways in which it can be measured; factors influencing the modality chosen in routine care and clinical trials; and the potential risks and benefits of plain radiography.

Of the 9 PRPs who participated (Supplementary Material 7, available with the online version of this article), 8 had had plain radiography of their hands and feet. Seven PRPs felt it was easy to undergo and that the time required was reasonable, although it was noted that it could be inconvenient to wait for the

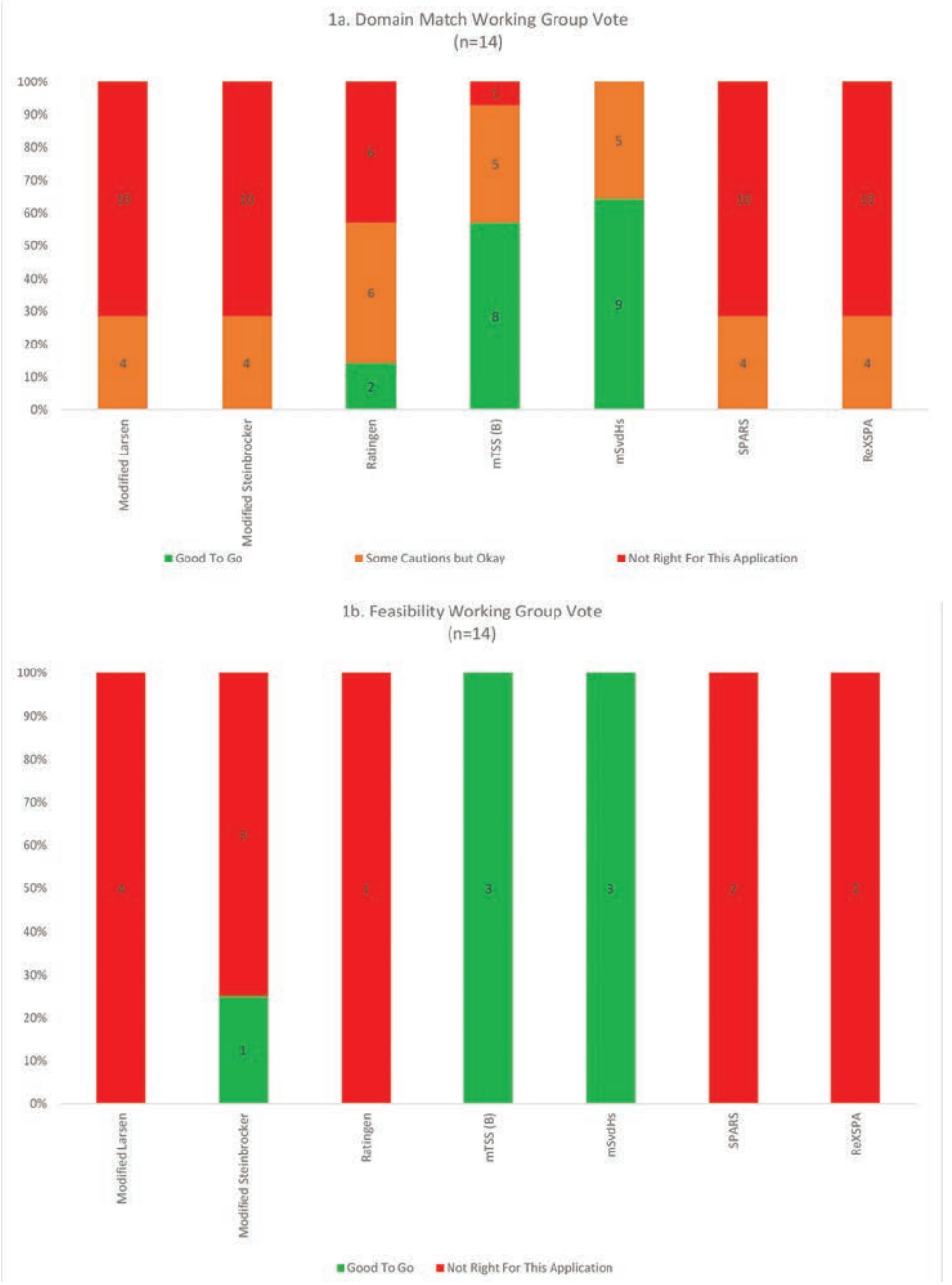

Figure 1. Working group voting results on instruments for (A) domain match and (B) feasibility. mTSS(B): modified total Sharp score, version B; mSvdHs: modified Sharp/van der Heijde score; ReXSPA: Reductive X-Ray Score for Psoriatic Arthritis; SPARS: Simplified Psoriatic Arthritis Radiographic Score.

imaging. Three PRPs (33%) were uncertain about the potential for harm of plain radiography, opining that the risks of radiation should be explained and that those risks may not be prohibitive. Three PRPs (33%) opined that there was a potential for discomfort in individuals with underlying joint pain or deformities. Two-thirds of PRPs felt that the costs were acceptable. Eight PRPs (89%) felt that there may be benefits to having plain radiography, but some commented that this might be the case in RCTs rather than at an individual level.

In the WG survey, 11 of 13 respondents felt it was easy to access plain radiography. After a first round of voting (n = 13), the results were discussed in an online meeting to optimize consensus. Many members who had utilized the instruments assessed felt that they were feasible; however, some expressed concern regarding the lack of a training platform or image atlas for the instruments. There was concern that this might affect the long-term fidelity of all instruments and negatively affect equitable access to radiographic scoring in centers where training is unavailable.

Following a second round of voting (n = 14, inclusive of 1 PRP), there was consensus (Figure 1B) that most instruments were AMBER based on the results of the initial survey balanced against the absence of training material (Supplementary

Table 1. Working group key discussion points on domain match and feasibility instruments.

Instrument	Domain Match			Feasibility		
	Results	Pros	Cons	Results	Pros	Cons
Modified Larsen	RED	• Includes JSN and erosions.	• Damage assessed as a composite outcome that predominately quantifies the percent of joint surface destroyed by erosions, but also includes features such as soft tissue swelling and osteoporosis. • Unable to demonstrate deterioration in existing JSN. • Wrist scored as a single joint.	RED	• No licensing fee. • No additional/ specialized equipment.	• Limited feasibility data. • No image atlas or formal training platform.
Modified Steinbrocker	RED	• Includes JSN and erosions. • Includes lysis, ankylosis, and subluxation.	• Damage assessed as a composite outcome that includes features such as soft tissue swelling and osteoporosis. • Unable to score JSN without erosive disease. • May miss a spectrum of disease between mild JSN/erosions and joint ankylosis/lysis. • Wrist scored as a single joint.	RED	• No licensing fee. • No additional/ specialized equipment. • Estimated training time available from previous feasibility exercise: 2 h to develop familiarity with the components and a further 50 h to score 100 radiographs covering a range of findings/severities with the supervision of a radiologist, followed by a blinded inter- and intrarater reliability exercise. • Time to score from previous feasibility exercise: 6.2 min.	• No image atlas or formal training platform.
Ratingen score	RED	• Includes erosions, ankylosis, and osteoproliferation.	• Does not include JSN. • Wrist scored as a single joint.	AMBER	• No licensing fee. • No additional/ specialized equipment. • Estimated training time available from previous feasibility exercise: 2 h to develop familiarity with the components and a further 50 h to score 100 radiographs covering a range of findings/ severity with the supervision of a radiologist, followed by a blinded inter- and intrarater reliability exercise.	• No image atlas or formal training platform. • Time to score from previous feasibility exercises: approximately 10 min.
mTSS-B	GREEN	• Includes JSN, erosions, ankylosis, and osteolysis. • Multiple carpal joints scored. • Utilized successfully in RCTs.	• Does not include osteoproliferation, which is a key feature of PsA, albeit slowly progressive. • Triquetrum can be difficult to assess.	AMBER	• No licensing fee. • No additional/ specialized equipment. • Estimated training time available from previous feasibility exercise: 2 h to develop familiarity with the components and a further 50 h to score 100 radiographs covering a range of findings/severity with the supervision of a radiologist, followed by a blinded inter- and intrarater reliability exercise.	• No image atlas or formal training platform. • Time to score from previous feasibility exercise: 14.6 min.

Table 1. Continued

Instrument	Domain Match			Feasibility		
	Results	Pros	Cons	Results	Pros	Cons
mSvdHs	GREEN	• Includes JSN, erosions, ankylosis, and osteolysis. • Multiple carpal joints scored. • Utilized successfully in RCTs.	• Does not include osteoproliferation, which is a key feature of PsA, albeit slowly progressive.	AMBER	• No licensing fee. • No additional/specialized equipment. • Estimated training time available from previous feasibility exercise: 2 h to develop familiarity with the components and a further 50 h to score 100 radiographs covering a range of findings/severity with the supervision of a radiologist, followed by a blinded inter- and intrarater reliability exercise.	• No image atlas or formal training platform. • Time to score from previous feasibility exercise: 14.4 min.
SPARS	RED	• Includes JSN, osteoproliferation, and erosions.	• Wrist scored as a single joint. • Each feature assessed in each joint as a binary outcome.	AMBER	• No licensing fee. • No additional/specialized equipment. • Estimated training time from developers: 4 h in clinicians familiar with plain radiography in PsA. • Time to score from previous feasibility exercise: 4.5 min.	
ReXSPA	RED	• Includes JSN, osteoproliferation, and erosions.	• Only radiocarpal joints scored in wrist. • Limited number of joints assessed.	AMBER	• No licensing fee. • No additional/specialized equipment. • Estimated training time extrapolated from previous feasibility exercise: 2 h to develop familiarity with the components and a further 50 h to score 100 radiographs covering a range of findings/severity with the supervision of a radiologist, followed by a blinded inter- and intrarater reliability exercise.	• Time to score not available.

JSN: joint space narrowing; mTSS-B: modified total Sharp score, version B; mSvdHs: modified Sharp/van der Heijde score; PsA: psoriatic arthritis; ReXSPA: Reductive X-Ray Score for Psoriatic Arthritis; RCT: randomized controlled trial; SPARS: Simplified Psoriatic Arthritis Radiographic Score.

Material 8, available with the online version of this article). The exceptions were the modified Steinbrocker and modified Larsen score, where 21% and 29% of respondents, respectively, felt that the instruments were not feasible, whereas > 70% of respondents felt both instruments could proceed with caution. It is important to note that the modified Steinbrocker has been utilized for decades to assess long-term structural damage in observational cohorts.

Conclusion

In the assessment of structural damage in peripheral PsA in RCTs evaluating a therapy against a comparator or a placebo, plain radiography is feasible and acceptable to individuals with PsA. The mSvdHs and mTSS-B have content validity (GREEN) and all instruments are potentially feasible (AMBER). Gaps highlighted are the need for instruments for large joints and the need for a training platform to optimize instrument feasibility. The next step will be to evaluate the measurement properties of the mSvdHs and mTSS-B in RCTs.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

REFERENCES

1. Orbai AM, de Wit M, Mease PJ, et al. Updating the psoriatic arthritis (PsA) core domain set: a report from the PsA workshop at OMERACT 2016. J Rheumatol 2017;44:1522-8.

2. Orbai AM, de Wit M, Mease P, et al. International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Ann Rheum Dis 2017;76:673-80.
3. Dures E, Hewlett S, Lord J, et al. Important treatment outcomes for patients with psoriatic arthritis: a multisite qualitative study. Patient 2017;10:455-62.
4. Kerschbaumer A, Baker D, Smolen JS, Aletaha D. The effects of structural damage on functional disability in psoriatic arthritis. Ann Rheum Dis 2017;76:2038-45.
5. Kane D, Stafford L, Bresnihan B, FitzGerald O. A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. Rheumatology 2003;42:1460-8.
6. Geijer M, Lindqvist U, Husmark T, et al. The Swedish early psoriatic arthritis registry 5-year followup: substantial radiographic progression mainly in men with high disease activity and development of dactylitis. J Rheumatol 2015;42:2110-7.
7. Ravindran J, Cavill C, Balakrishnan C, Jones SM, Korendowych E, McHugh NJ. A modified Sharp score demonstrates disease progression in established psoriatic arthritis. Arthritis Care Res 2010;62:86-91.
8. Touma Z, Thavaneswaran A, Chandran V, Pellett F, Cook RJ, Gladman DD. Clinical and demographic characteristics of erosion-free and erosion-present status in psoriatic arthritis in a cohort study. J Rheumatol 2016;43:1057-62.
9. Siannis F, Farewell VT, Cook RJ, Schentag CT, Gladman DD. Clinical and radiological damage in psoriatic arthritis. Ann Rheum Dis 2006;65:478-81.
10. Bond SJ, Farewell VT, Schentag CT, Gladman DD. Predictors for radiological damage in psoriatic arthritis: results from a single centre. Ann Rheum Dis 2007;66:370-6.
11. Gladman DD, Farewell VT, Wong K, Husted J. Mortality studies in psoriatic arthritis: results from a single outpatient center. II. Prognostic indicators for death. Arthritis Rheum 1998;41:1103-10.
12. Landewe R, Ritchlin CT, Aletaha D, et al. Inhibition of radiographic progression in psoriatic arthritis by adalimumab independent of the control of clinical disease activity. Rheumatology 2019;58:1025-33.
13. Coates LC, Helliwell PS. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. Arthritis Care Res 2010;62:965-9.
14. Helliwell PS, Kavanaugh A. Radiographic progression in psoriatic arthritis achieving a good response to treatment: data using newer composite indices of disease activity. Arthritis Care Res 2018;70:797-800.
15. Taylor WJ, Porter GG, Helliwell PS. Operational definitions and observer reliability of the plain radiographic features of psoriatic arthritis. J Rheumatol 2003;30:2645-58.
16. Antony A, Holland R, D'Agostino MA, et al. Measurement properties of radiographic outcome measures in psoriatic arthritis: a systematic review from the GRAPPA-OMERACT initiative. Semin Arthritis Rheum 2021;51:367-86.
17. Mease PJ, Kivitz AJ, Burch FX, et al. Continued inhibition of radiographic progression in patients with psoriatic arthritis following 2 years of treatment with etanercept. J Rheumatol 2006;33:712-21.
18. Gladman DD, Mease PJ, Ritchlin CT, et al. Adalimumab for long-term treatment of psoriatic arthritis: forty-eight week data from the adalimumab effectiveness in psoriatic arthritis trial. Arthritis Rheum 2007;56:476-88.
19. Simonic E, Peternel S, Stojnic-Sosa L, et al. Negative and positive life experiences in patients with psoriatic arthritis. Rheumatol Int 2013;33:1587-93.