Inflammation as a target for treatment in hand osteoarthritis

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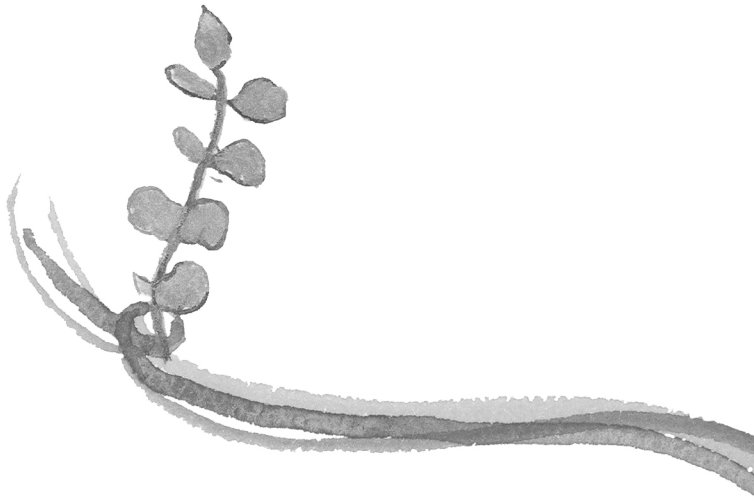
CHAPTER 13

Report from the Hand Osteoarthritis Working Group at OMERACT 2018: update on core instrument set development



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ABSTRACT

Objective. To evaluate hand osteoarthritis tools for core instrument set development.

Methods. For OMERACT2018, a systematic literature review and advances in instrument validation were presented.

Results. Visual analog and numerical rating scales were considered valuable for pain and patient's global assessment, despite heterogeneous phrasing and missing psychometric evidence for some aspects. The Modified Intermittent and Constant Osteoarthritis Pain scale was lacking evidence. The Michigan Hand Outcomes Questionnaire had advantages above other pain/function questionnaires. The Hand Mobility in Scleroderma scale was valid, although responsiveness was questioned. Potential joint activity instruments were evaluated.

Conclusion. The development of the core instrument set is progressing, and a research agenda was also developed.

INTRODUCTION

Hand osteoarthritis (OA) is a highly prevalent disorder, causing a considerable burden of disease.[1] Simultaneous involvement of multiple hand joints and presence of different subsets (e.g., nodal, thumb base, and erosive OA) make it difficult to study. To advance our understanding, high-quality studies with optimal outcome measurement are essential.

The Outcome Measures in Rheumatology (OMERACT) Hand OA Working Group (WG), assembled in 2010, endorsed a core domain set for clinical trials of symptom and structure modification and observational studies at OMERACT 2014,[2] which was included in the Osteoarthritis Research Society International recommendations for design and conduct of clinical trials in hand OA.[3] The core domain set includes 6 domains for all settings [pain, physical function, patient's global assessment (PtGA), health-related quality of life (HRQOL), joint activity, and hand strength], and 2 additional domains for trials of structure modification and observational studies (hand mobility and structural damage). HRQOL and hand mobility are not mandatory domains.

A preliminary core instrument set was also proposed including visual analog (VAS) or numerical rating scales (NRS) for pain, Functional Index for Hand OA (FIHOA), tender joint count, and pinch/grip strength.[2] Subsequent goals of the WG were to (1) evaluate relevant instruments according to The OMERACT Handbook,[4] and (2) update the research agenda on the final core instrument set selection.[5] Progress was discussed at OMERACT 2018.

METHODS

Instrument and domain selection

The selection of instruments and domains presented and discussed at OMERACT 2018 were based on the needs addressed in the previous research agenda. Several discussions among members of the hand OA WG were held during the annual meetings of European League Against Rheumatism (2016, 2017) and the American College of Rheumatology (2017) and during a telephone conference organized by the steering committee (April 2017) prior to OMERACT 2018 to guide the program of the special interest group meeting (SIG).

Review of instruments measuring pain and PtGA

A systematic literature review (SLR) was performed (RW, BK, AA) including studies reporting on hand pain and PtGA measured on VAS or NRS in patients with hand OA. A previous SLR on measurement properties of pain and function instruments in hand OA until January 2014 was used as a basis.[6] Relevant manuscripts from that SLR were extracted. Additionally, medical literature databases (Pubmed, Embase, Web of Science, COCHRANE, CINAHL, Academic Search Premier, ScienceDirect) were searched from January 2014 to January 2018 applying similar methodology as the 2014 SLR (see supplementary file). Psychometric features of the scales, such as reliability, responsiveness, construct validity, and clinical trial discrimination, were extracted and evaluated according to The OMERACT

Handbook.[4] These features were discussed at OMERACT 2018 during the SIG meeting that was attended by 24 participants representing clinicians, researchers, patients, and regulatory authorities.

Special attention was given to the phrasing and other details of the VAS/NRS question.

Construct validity of the modified Intermittent and Constant OA Pain (ICOAP; IKH)[7-9] was studied in the Nor-Hand study to investigate whether constant and intermittent pain were separate constructs in hand OA.

Investigation of other potential core instruments

Work was conducted by WG members on the relevant validity and psychometric properties of other tools: (1) properties of the Michigan Hand Outcomes Questionnaire (MHQ; FK)[10,11] were compared to more commonly used hand OA questionnaires, specifically the Australian/Canadian Hand OA Index (AUSCAN) and FIHOA[12,13]; (2) performance of Hand Mobility in Scleroderma (HAMIS) and its responsiveness was compared to other mobility instruments (FK)[14]; (3) assessment of tender joint count to measure joint activity (FK).[15,16]

Research agenda

Guided by discussions prior to and at OMERACT 2018, a research agenda was developed.

RESULTS

Domain pain and PtGA: progress in instrument validation

From the previous SLR, 32 relevant manuscript were selected, providing data on VAS/NRS pain and/or PtGA.[6] Since January 2014, 18 relevant manuscripts were published and could be added (S1-S50, see reference list in supplementary file). Details of all included manuscripts can be found in supplementary table 1. Summary results of the search (supplementary figure 1) and psychometric features of both scales within these domains were discussed by the WG (table 1). VAS range 0-100 mm was the most studied scale (in 26/46 studies for pain and 10/15 studies for PtGA). No study reported test-retest reliability data on the use of either scale in these domains. For pain, good construct validity of VAS was shown (S3,S24,S50), while only limited data were available for NRS (S41). Twenty-two (S1,S2,S4,S6-S13,S15-S18,S21,S22,S26,S37,S38,S42 ,S46) and 8 studies (S15,S25,S28,S33,S34,S41,S45,S47) showed evidence for responsiveness of VAS and NRS, respectively, and 13 (S7-S12,S17,S21,S22,S26,S37,S38,S46) and 6 studies (S14,S28,S33,S34,S41,S47) for clinical trial discrimination for VAS and NRS, respectively.

For PtGA, construct validity was not studied. Evidence to support responsiveness for VAS was available in 10 studies (S3,S6,S12,S13,S15,S18,S22,S29,S38,S40), and 3 studies for NRS (S14,S28,S45) . The capacity to discriminate in clinical trials was shown for VAS PtGA in agreement with the primary outcome in 5 studies (S12,S22,S29,S38,S40), while only 1 study supported this for NRS (S28).

Strikingly, phrasing of the question accompanying VAS/NRS in both domains was very heterogeneous, and details were often not reported. For pain, substantial variety existed in which aspect(s) of pain were assessed (e.g., pain at rest or upon exertion, average or worst pain), location and joint(s) referred to (e.g., target joints, dominant hand, both hands) and time of recall (undefined or ranging from current to 2 weeks; supplementary table 2). Similarly, for PtGA, time of recall was undefined in most studies (3/15 studies did specify; all 48 h; supplementary table 3). After presentation of these findings at OMERACT 2018, the WG proposed that clear standardized phrasing accompanying these instruments should be defined for pain and PtGA. It was proposed that PtGA should assess the effect of the disease on the patient's general well-being. Review of results of previously held focus groups was suggested to analyze what is most relevant to patients.[17]

Results of the validation study of the modified ICOAP were discussed at OMERACT 2018. Detailed results are presented elsewhere.[9] In short, in patients with hand OA, constant and intermittent pain largely overlapped and were not separate constructs, in contrast to the situation in knee and hip OA.[7,8] The existence of separate constructs in hand OA seemed clinically plausible but might be influenced by hand OA location (finger vs thumb base) and involvement of multiple hand joints at different disease stages. It was suggested to seek more patient input, since the development of ICOAP was based on focus group discussions with patients with knee and hip OA, but not hand OA. However, previous focus groups of patients with hand OA have already identified a range of pain concepts, such as fluctuating pain and psychological consequences of pain, which are not represented in the commonly used instruments to assess hand OA.[17]

Based on the available evidence, it was concluded that VAS and NRS are most likely the best instruments to measure pain and PtGA. However, evidence about some essential psychometric properties is missing, in particular regarding reliability, construct validity for NRS pain/PtGA, and clinical trial discrimination for NRS PtGA.

Evaluation of other potential core instruments and research agenda

The results of comparison of MHQ with AUSCAN and FIHOA for measuring domains pain and function were discussed in light of OMERACT Filter 2.1 (table 2).[4,10-13] While displaying similar measurement properties, important advantages of MHQ above other instruments were that it can overcome issues of copyright (AUSCAN) and outdated questions (FIHOA). The possibility to propose more than 1 instrument for a core domain, with the accompanying risk of jeopardizing standardization, was discussed.

Assessment of HAMIS performance in comparison to other mobility instruments was published previously.[14] Though HAMIS appeared the most useful to measure hand mobility compared to other instruments, the WG debated that responsiveness data are weak. Over a 2-year period, limited change over time was observed,[14] either indicating that the domain itself does not change, or that the instrument cannot detect this change.

Table 1. Metric properties of VAS and NRS measuring pain and patient global assessment (PGA): construct validity, reliability, longitudinal construct validity (responsiveness) and clinical trial discrimination.

Domain	Scale	Construct validity	Reliability	Longitudinal construct validity (responsiveness)	
		Studies showing significant correlation with:	No. studies	No. studies showing change	No. studies showing no change, in disagreement with other outcomes
Pain	VAS	AUSCAN pain: r = 0.77-0.81 (S3, S24, S50)	0	22 (S1,S2,S4,S6-S13,S15-S18,S21, S22,S26,S37,S38, S42,S46)*	3 (S31,S39,S44)
	NRS	AUSCAN pain: R^2 = 0.606 (S41) AUSCAN function: R^2 = 0.471 (S41)	0	8 (S15,S25,S28, S33,S34,S41,S45, S47)	0
PGA	VAS	0	0	10 (S3,S6,S12, S13,S15,S18,S22, S29,S38,S40)*	0
	NRS	0	0	3 (S14,S28,S45)	0

*Saviola et al., 2017 (S38): no hard data shown, only described in full text. S(number): refers to the reference in the Supplementary reference list. VAS, visual analog scale; NRS, numeric rating scale; AUSCAN, Australian/Canadian Hand OA Index; r, coefficient of correlation; R^2, correlation.

	Clinical trial discrimination			
Percentage of studies that detected change	No. studies showing discrimination between arms in agreement with primary outcome	No. studies not showing discrimination between arms in agreement with primary outcome	No. studies showing discrimination between arms in disagreement with primary outcome	No. studies not showing discrimination between arms in disagreement with primary outcome
88	13 (S7-S12,S17, S21,S22,S26, S37,S38,S46)	6 (S1,S5,S6, S23,S32,S44)	2 (S13,S42)	7 (S15,S19,S30, S39,S43,S48, S49)
100	6 (S14,S28,S33, S34,S41,S47)	0	1 (S16)	1 (S25)
100	5 (S12,S22,S29, S38,S40)	2 (S6,S40)	1 (S15)	0
100	1 (S28)	0	0	1 (S14)

Table 2. Comparison of properties of Michigan Hand Outcomes Questionnaire (MHQ), Australian/Canadian Hand Osteoarthritis Index (AUSCAN), and Functional Index for Hand Osteoarthritis (FIHOA).

Variables	MHQ[10]
Domain: Pain	
No. items	5
Floor and ceiling effects*	No (1.8% with lowest score, 0% with highest score)
Aspect of pain assessed	Frequency of experiencing pain in several situations (in general, during sleep or ADL) and whether it affects the respondent's happiness.
Specific other comments	No
Domain: Function	
No. items	Overall hand function scale: 10; ADL scale: 17
Floor and ceiling effects*	No (subscales overall hand function/ADL: 0%/0% with lowest score, 1.3%/3.1% with highest score)
Aspect of function assessed	Overall hand function scale: general questions of hand function, movement, strength and sensation. ADL scale: ability to perform certain tasks (turning doorknob, picking up coin, holding glass of water, turning key in lock, holding heavy object with one hand, opening jar, buttoning shirt, using cutlery, carrying large and heavy objects, washing dishes, washing hair, tying shoelaces or knots); 4/12 grip strength tasks, 3/12 fine motor skills tasks.
Specific other comments	Separate assessment of left and right hand.
General aspects	
Recall period	1 week
Other available subscales (domain)	Work performance (N/A); aesthetics (structural damage); satisfaction (N/A)
Total no. items	58
Method of scoring	Includes normalizing to 0-100 scale, presented in user manual
Costs	Freely available for academic or non-profit institutions, permission needed before use (online application form)
Available in multiple languages	Yes
Interpretability comments	Pain scale has to be interpreted in opposite direction compared to other subscales

*Data reviewed in HOSTAS cohort (n = 383), Leiden University Medical Center, Leiden, the Netherlands. ADL, activities of daily living; N/A, not available; VAS, visual analog scale.

	AUSCAN[12]	FIHOA[13]
	5	-
	No (1.8% with lowest score, 1.3% with highest score)	-
	Pain severity during rest and several tasks (lifting, squeezing, turning, gripping)	-
	No	-
	9	10
	No (1.8% with lowest score, 0.3% with highest score)	No (4.2% with lowest score, 0% with highest score)
	Ability to perform certain tasks (turning doorknobs, holding heavy object with one hand, buttoning shirt, using cutlery, carrying large and heavy objects, turning taps, fastening jewelry, wringing cloth); 4/9 grip strength tasks, 2/9 fine motor skills tasks.	Ability to perform certain tasks (turning key in lock, holding heavy objects, buttoning shirt, using cutlery, tying shoelaces or knots, cutting with scissors, clenching fist, sewing (women) / using screwdriver (men), writing for a long time, accepting a handshake); 1/10 grip strength tasks, 4/10 fine motor skills tasks.
	No	Some items may be culturally challenging (accepting a handshake), or outdated (writing for more than 10 minutes; women sew and men use a screwdriver)
	48 h	Not specified
	Stiffness (N/A)	N/A
	15	10
	Dependent on version used (Likert scale, VAS), presented in user manual	Simple addition of scores, user guide available online
	Copyrighted, payment of fee and permission needed before use	No
	Yes	Yes
	No	No

Table 3. Future research agenda to promote core instrument set selection for hand OA.

- Definition of standardized phrasing for VAS and NRS pain and PGA
- Assessment of test-retest reliability of VAS and NRS pain and PGA
- Investigation of construct validity for NRS pain and PGA, and discriminative capacity in clinical trials for NRS PGA
- Investigation of validity of combinations of instruments to assess joint activity, including e.g., tender joints, self-reported painful joints, swollen joints, pain while gripping, and inflammatory signs on imaging
- Assessment of reliability of soft tissue joint swelling in hand OA
- Investigation of psychometric properties of grip and pinch strength to measure core domain hand strength
- Review of available instruments to assess health-related quality of life in hand OA, and development of a disease-specific instrument
- Investigation of the metric properties of ultrasound and magnetic resonance imaging
- Investigation of the value of computer tomography

OA, osteoarthritis; VAS, visual analog scale; NRS, numerical rating scale; PtGA, patient's global assessment.

Progress in instrument development for joint activity is published in conference abstracts.[15,16] Lack of a well-accepted definition hampers instrument development for this domain. Potential instruments include ultrasound and magnetic resonance imaging to detect inflammation, palpation to reveal pain, self-reported painful joint count, soft tissue swelling, and pain while gripping. In the WG discussion, it was suggested that some instruments complement each other, and a combination may be useful. Prediction of radiological progression was proposed as an anchor to assess suitable instruments.

Following discussion of these results, an agenda was developed to guide future research (table 3).

DISCUSSION

Progress results were presented and discussed regarding the development of a core instrument set for hand OA. The core instrument set was developed through investigation of the psychometric properties of candidate instruments according to The OMERACT Handbook,[4] assessing construct validity, reliability, responsiveness, and clinical trial discrimination. The results serve as the basis of an updated research agenda.

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