Ankylosing Spondylitis: Plenary Discussion and Results of Voting on Selection of Domains and Some Specific Instruments

Participants of the OMERACT Conference received the aims and outline of the ankylosing spondylitis (AS) module before the meeting, together with the key paper on selection of domains by the Assessments in Ankylosing Spondylitis (ASAS) Working Group, as well as a summary of the consensus procedure on selection of specific instruments[1,2]. After presentation of the papers in the plenary session, followed by selection of a core set based on cluster analysis, the audience was given the opportunity to discuss the presented data[3]. The majority of the audience agreed on the proposed core sets by the ASAS Working Group and on the selection of the specific instruments. A few items were brought for amendment. One important issue was the domain "fatigue." This was put on the list as a potentially important domain for the disease controlling antirheumatic therapy (DC-ART) core set, but was left out during the further process of selection of specific instruments because no available instrument was considered relevant by more than 50% of the ASAS members[2]. The audience strongly recommended that despite this, fatigue should remain on the research agenda. Another item brought for amendment, "entheses," had been included under the domain "peripheral joints and entheses"; however, no specific instrument was recommended to assess the entheses, because again no available instrument was considered relevant by at least 50% of the ASAS members. Some participants judged enthesopathy as one of the 4 key areas in AS: axial involvement, peripheral joints, extraspinal and extraarticular manifestations, and enthesopathy. It was decided that further research should be done on instruments to assess involvement of entheses in AS, an important and rather specific feature of AS (Table 1).

To ensure uniformity between the core sets for the various settings, it was concluded that a common core should be defined for all 3 settings. This core was the set defined for the symptom modifying antirheumatic drugs (SMARD)/ physical therapy setting. In addition, a few other domains were to be added for clinical record keeping and other domains for the DC-ART setting. This could be achieved by defining domains "spinal stiffness" and "acute phase reactants" (not originally included definitely by the ASAS group) unconditionally in the core set for DC-ART. Figure 1 shows the included domains for the 3 settings. Also, the process and the results of the selection of the specific instruments were endorsed by the audience as a starting point for further research[2]. Thereafter an attempt was made to address the remaining issues about preferences for either erythrocyte

Table 1. Specific instruments for each domain in core sets for DC-ART, SMARD, physical therapy, and clinical record keeping.

Domain	Instrument
Function*	BASFI or DFI
Pain*	VAS–last week–spine–at night–due to AS
	AND VAS–last week–spine–due to AS
Spinal mobility*	Chest expansion
	AND modified Schober
	AND occiput to wall
Patient global*	VAS–last week
Stiffness*	Duration of morning stiffness–spine–last week
Peripheral joints**	No. of swollen joints (44 joint count)
Entheses**	No preferred instrument available
Acute phase reactants**	ESR
Xray spine	AP + lat lumbar
	AND lat cervical spine
	AND X-pelvis (SI and hips)
Xray hips	See spine
Fatigue	No preferred instrument available

*Included in all 3 core sets for DC-ART, SMARD/physical therapy, and clinical record keeping.
**Included in core sets for DC-ART and clinical record keeping.
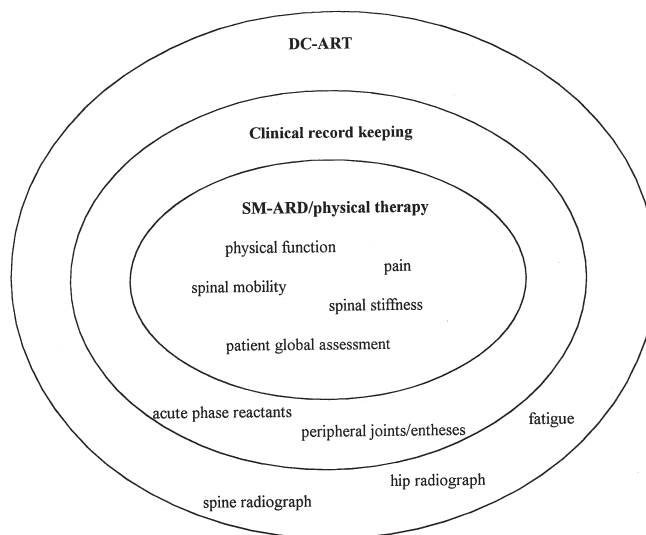SI: sacroiliac joint.

Figure 1. Domains of the core sets for SMARD/physical therapy (inner circle), clinical record keeping (2 inner circles), and DC-ART (all 3 circles) as endorsed by ASAS/OMERACT/ILAR.

sedimentation rate (ESR) or C-reactive protein (CRP) and preferences for either the Bath Ankylosing Spondylitis Function Index (BASFI) or Dougados Functional Index

(DFI)[4,5]. Both sessions started with a review of current literature on these assessments, followed by the presentation of new research data[6–10]. The final section dealt with available scoring methods to assess damage in AS by radiography. All 3 sessions were followed by a plenary discussion and the participants had the opportunity to vote on various issues.

ESR versus CRP

The following conclusions were drawn for ESR and CRP. Both acute phase reactants are moderately associated with aspects of disease activity such as signs of inflammation and range of motion, as well as damage. Subgroups defined according to clinical variables (such as spinal disease only versus spinal disease together with peripheral joints) show differences in (mean) ESR and (mean) CRP. Acute phase reactants explain some aspects of disease activity, but there are insufficient data on their etiopathological significance. Applying the OMERACT filter, data show that both ESR and CRP fulfil some aspects of truth and discrimination. It was agreed that in AS we indeed need to measure an acute phase reactant during followup of the disease. However, not enough data from longitudinal studies are currently available on longterm discriminative power or on the predictive value of elevated ESR or CRP values. In available data there are no real differences in performance between ESR and CRP. Therefore aspects of feasibility are important when choosing between the two. The participants advised measuring ESR whenever possible since it is inexpensive and this measure can also be included in the core set for longitudinal and observational studies[11]. Sometimes CRP is preferred for logistic reasons, for example when a central laboratory is used in a multicenter trial. It was urgently requested that ESR be performed in such cases also (e.g., in the local laboratory) to ensure comparability of studies. Important issues for further research are the predictive value, and aspects of truth and longitudinal discrimination. Further comparisons between ESR and CRP were not considered relevant.

BASFI versus DFI

From the presented data it was obvious there were few differences between the two functional indexes. The majority of participants voted that it was unnecessary to choose between them. Both are feasible and fulfil some aspects of the truth and discrimination criteria of the OMERACT filter. Additional testing is needed for BASFI in the DC-ART setting. Also, explicit rules on how to handle missing items in both scales are needed.

Several suggestions were made to advance research within this field in AS. (1) It was suggested to evaluate differences in misclassified patients (misclassified as having high or low disease activity and/or damage), especially patients misclassified by one but not by the other instrument. Does this depend on specific questions within the questionnaires? (2) To merge the two instruments and make one large pool of questions. (3) The calibration of the two instruments could be undertaken by means of a Rasch analysis[12,13]. This can be done if both instruments measure the same underlying construct. Calibration of the instruments would be a way not to dismiss one measure, but to use both instruments independently and to calculate and translate the results of the different instruments. (4) It would also be interesting to evaluate the influence of changing answer modalities. Because visual analog scales may have problems (e.g., in some cultures), it would probably be good to test the BASFI with a Likert scale. Both BASFI and DFI could also be tested using numerical rating scales, as these have some advantages over other types of answer modalities[14]. The final decision by participants was that both instruments be used for the time being, but that additional research was needed to collect additional data on the instruments and improve them further if possible and/or necessary.

RADIOGRAPHIC SCORING METHODS

Over all, it was felt to be a very important but neglected issue to state the purpose of a scoring method, e.g., to measure the natural course of disease or to evaluate a specific therapeutic intervention. One scoring method might be preferable in one study, another method might be preferred in another, depending on the specific aims of that study. Not enough data are available on the exact relation between disease activity and the occurrence of damage. Indeed, there are several types of damage. Possibly some features assessed as damage are in fact results of healing (syndesmophytes?). The relation between pathophysiologic mechanisms and the occurrence of specific features on radiographs should be the subject of further research. It might also be helpful to look for relations between specific clinical and radiographic features. This type of research could lead to the development of an entirely new scoring system. Some participants suggested the development of a separate score for proliferation of bone and for destruction of bone.

Vote results showed the majority of the participants judged both the Bath Ankylosing Spondylitis Radiology Index (BASRI)[15] and the Stoke Ankylosing Spondylitis Spine Score (SASSS)[16] as feasible methods. However, no method could pass the OMERACT filter for truth or discrimination. But the audience agreed that additional evaluation of both methods on aspects of truth and discrimination would be appropriate. There was divided opinion on whether a new scoring method should be started "from scratch." Extra research is hampered by the lack of a good external standard. Magnetic resonance imaging (MRI) might be helpful in unravelling the meaning of the various features on radiographs.

CONCLUSION

The preparatory work done by the ASAS group was endorsed by OMERACT and ILAR after slight modifica-

tion. Now a core of domains is available for all settings; this needs to be extended for clinical record keeping and for the evaluation of a DC-ART. In the selection of the specific instruments, the main amendment is that both fatigue and entheses remain on the item list, even though at the moment no good instruments seem to be present to assess these issues. Differences regarding the OMERACT filter are minimal between ESR and CRP. Based on feasibility aspects, ESR is preferred and should be included in each study. Both BASFI and DFI can be used. Further research will be started, e.g., to calibrate the instruments, then the results of the two instruments can be used together. The two available radiographic scoring methods are feasible, but much research is still needed on the aspects of truth and discrimination. The development and evaluation of a new scoring method might be necessary.

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