ARD Online First, published on August 23, 2017 as 10.1136/annrheumdis-2017-211433

EXTENDED REPORT

The effects of structural damage on functional disability in psoriatic arthritis

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Handling editor Tore K Kvien

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/annrheumdis-2017-211433).

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Received 7 March 2017
Revised 28 July 2017
Accepted 31 July 2017

ABSTRACT

Background Functional outcomes are central in patients with chronic inflammatory musculoskeletal diseases. In a secondary data analysis of the GO-REVEAL trial (NCT00265096), we investigated wether structural damage is linked to functional impairment in patients with psoriatic arthritis (PsA), a link that is still elusive in this disease.

Methods We analysed 363 patients enrolled in the GO-REVEAL study and obtained modified Sharp/van der Heijde Scores (mSvdHS) from X-rays performed at baseline, after 24, 52 and 104 weeks. Using longitudinal analyses, we assessed the effect of total mSvdHS (and its subscores, joint space narrowing (JSN) and erosions (ERO)) on functional status (measured by the Health Assessment Questionnaire) in all patients and in those attaining remission (n=117). Furthermore, we analysed wether structural damage reduces the responsiveness of functional limitations to treatment in a subgroup of responders who had functional impairment at baseline (n=67). Additionally, internal and external validation analyses were performed.

Results The effect of damage on function was seen in the disease activity-adjusted models using total mSvdHS (p=0.005), JSN (p=0.019) and ERO (p=0.001) as well as in the remission analyses for mSvdHS (p=0.029) and JSN (p=0.010), respectively. Functional responsiveness was limited by increasing total mSvdHS (p=0.010), JSN (p=0.002) and ERO (p=0.040). The results were validated using other functional outcomes and in an independent clinical cohort.

Conclusions In PsA, structural damage, particularly JSN, has implications for physical function. Functional outcomes have an irreversible component that is strongly related to the extent of joint destruction. This needs to be considered when targeting functional outcomes in clinical practice.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects the musculoskeletal system in multiple ways. Aside from overt peripheral arthritis, inflammation of entheses and the axial skeleton, is part of the disease spectrum. Particularly, the inflammatory process of the peripheral joints can lead to substantial cartilage and bony destruction, but also bony overgrowth.[1] While physical function is strongly affected by the active inflammatory process that leads to pain, swelling and stiffness ('disease activity'), it is conceivable that also the aforementioned joint damage leads to functional limitations over time. Similar to rheumatoid arthritis (RA),[2] disease activity is associated with joint damage in PsA.[3] Moreover, in RA,[4 5] there is also a well-established link between structural damage and disability, and this link is even tighter for cartilage damage than for bony damage.[6] Although peripheral joint damage is generally greater in RA than in PsA,[7] there is still evidence for some association of joint damage with disability in the latter.[3] This is indicated by larger functional impairment with increasing disease duration but not necessarily conclusive results regarding damage.[8]

Here, we investigated in detail if and to what extent joint destruction and functional status are linked in patients with PsA. The results of this study should therefore allow to estimate the functional impact of structural damage in PsA. Also, we investigated to what extent functional improvement is limited by fixed, damage-related functional components, and whether this is related to changes of cartilage or bone.

METHODS

Patients and assessments

In the present study, we performed a secondary analysis on patients who had been enrolled in the Golimumab — A Randomized Evaluation of Safety and Efficacy in Subjects with Psoriatic Arthritis Using a Human Anti-TNF Monoclonal Antibody (GO-REVEAL) study (trial registration number: NCT00265096) comparing golimumab with placebo in 405 patients with PsA.[9] The institutional review boards and ethics committees of all participating centres had approved the study and informed consent of all patients included in the GO-REVEAL trial were obtained prior to study participation. The sponsor limited the provision of patient level data to a random cut of 90% for our secondary data analyses. Among the patients, 43% had polyarticular and 57% had oligoarticular disease. We extracted modified Sharp/van der Heijde Scores (mSvdHS),[10 11] by which the structural damage was quantified in the trial at baseline and after 24, 52 and 104 weeks in all patients (n=363). The mSvdHS is based on scoring of erosions (ERO) and joint space narrowing (JSN), with a maximum score of 320 for ERO and 208 for JSN, resulting in an mSvdHS ranging from 0 to 528.[10] The smallest detectable change in the GO-REVEAL trial was 1.56 for the total score, 1.18 for ERO and 0.96 for JSN.[9] For assessment of disease activity, we calculated the Disease Activity Index for Psoriatic Arthritis (DAPSA),[12] which allows a metric quantification of disease activity at every clinical visit (DAPSA=SJC66+TJC68+Patient Global (0–10)+Patient Pain (0–10)+CRP (mg/

To cite: Kerschbaumer A, Baker D, Smolen JS, *et al*. *Ann Rheum Dis* Published Online First: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2017-211433

dL)). Functional status was assessed using the traditional Health Assessment Questionnaire (HAQ) disability index, which has been commonly used in PsA.[3 13–16]

Influence of disease activity on physical function

As a first step, we evaluated the association of disease activity with the HAQ, in line with a similar previous analysis.[17] To this end, a longitudinal data model using generalised estimating equations (GEE) was developed. The GEE methodology provides the possibility to take multiple observations of each individual patient into account and simultaneously allows to adjust for different independent variables (e.g. disease activity, X-ray score) of each patient's observation. As HAQ, disease activity and radiographic scores may change across each patient's study visit, statistical methods as the GEE method allow to account for this aspect and provide overall effect associations, while adjusting for changes on an individual patient level.

In our analyses, HAQ was used as the outcome variable, with visit and DAPSA as independent variables. An autoregressive variance–covariance correlation matrix (AR(1)) was chosen based on the best GEE Fit Criteria.[18]

Since in a state of low disease activity (LDA), minor changes of disease activity may influence physical function more than in high disease activity states, we used a multistep approach including also quadratic and cubic terms of DAPSA in the model. While the cubic term did not show significant results, the quadratic model did and was therefore chosen for analysis of the influence of disease activity on physical function.

Influence of structural damage on physical function

For analysis of the effects of structural damage on functional disability, we used all visits of all patients that had HAQ, X-ray score and DAPSA available, that is, baseline and weeks 24, 52 and 104. Among the visits of all 363 patients, 1286 of 1322 visits (97.3%) were used, with 32 visits (2.7%) being excluded because of missing values (of HAQ, mSvdHS or DAPSA). Data were missing completely at random.

Again, we used a GEE longitudinal analysis on all patients. HAQ of each visit was used as dependent variable and mSvdHS, JSN or ERO, respectively, were used as independent variables in separate models (with total mSvdH, ERO and JSN score separately included in each model). In all GEE models, since the dependent variable (HAQ) appeared normally distributed, normal distribution with the identity link function was chosen, as well as an autoregressive correlation matrix, to account for patients' within-subject correlations over time. We adjusted the model for DAPSA scores, given the expected substantial effects of disease activity on functional scores.

The effects of disease activity on function may by far exceed the effect of structural damage on function, which might pose a problem when adjusting for this major effect statistically. We therefore also developed a model which included only the subgroup of patients who had at least one visit in DAPSA remission (n=117). We used all remission visits of these patients, in total 213, in a longitudinal model as above, with the exception that no adjustment for DAPSA was needed, given absence of active disease in the selected remission visits. Remission was defined as a DASPA of ≤4.[19]

To investigate further how damage would influence other response measures of disease activity (patient global assessment of disease activity, evaluator global assessment of disease activity, patient global assessment of pain, SJC66, TJC68), similar models as in the remission analyses were developed, using these measures as dependent variables (instead of HAQ) in separate models in the DAPSA remission cohort.

To put these results into clinical context, we also evaluated how many patients achieving DAPSA LDA (DAPSA ≤14) in each tertile of mSvdHS were able to achieve a 'normal' HAQ of <0.5 at week 52.[20] To compare the risk of HAQ normalisation between the groups, the risk ratio (RR) between the first and third tertile was calculated. Additionally, the absolute risk reduction (ARR) and number needed to treat (NNT) were calculated. Differences were compared using the χ^2 test; group differences of continuous group characteristics (disease duration, age, DAPSA at baseline, HAQ at baseline) were compared using unpaired t-tests.

Influence of structural damage on functional responsiveness

Finally, we tested the following hypothesis: if structural damage (which is presumed to be irreversible) explains parts of the functional disability in patients with PsA, then patients with a higher degree of structural damage should be expected to have a smaller functional responsiveness to therapy than those with less or no damage, leading to a floor effect of physical function, preventing further improvement beyond that point. To confirm the hypothesis that such an 'irreversible' component of disability exists in PsA, we used a longitudinal GEE model in which we assessed the effect of radiographic damage (corresponding to this putative irreversible functional component) on changes in HAQ from baseline, while adjusting for HAQ at baseline. We performed this analysis on a subgroup of patients who showed a major response of DAPSA (improvement of ≥85%) from baseline,[19] and who had a baseline HAQ≥1 (since patients with normal or near normal function at baseline would not be informative in this analysis of functional responsiveness).

Validation

To show the independence of the results from the measurement instrument used for physical function assessment, we also performed the remission and responsiveness analyses using the Physical Component Score of the 36-Item Short Form Survey Instrument (SF-36 PCS), instead of HAQ and HAQ change, as outcome variable in GO-REVEAL patients.[14 21]

Since the above analyses were based on one patient cohort, we externally validated these data using a clinical database of routine patients seen at our clinics. The use of PsA patient data was approved by the ethics committee of the Medical University of Vienna (EK Nr: 2002/2014). In total, our X-ray database includes visits of 206 PsA patients. We identified all PsA patients (n=160) who had complete cDAPSA (the clinical version of the DAPSA without C reactive protein),[19] HAQ assessment and a corresponding radiographic assessment at or within 6 months of the clinical remission visit. Fifty-five (34.4%) of these patients achieved cDAPSA remission in the course of their disease. Respective dropout numbers are provided in the online supplementary table S3. An experienced scorer (GS), blinded to the purpose of this study, scored all radiographs of all identified patients. In this cohort, the same model as described above for the overall and the DAPSA remission cohort was used.

All analyses were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

Patient characteristics

The baseline characteristics of the 363 patients extracted from the trial cohort are presented in table 1, together with

the corresponding characteristics of the subsets of patients for the remission analysis (n=117) and the response analysis (n=67). For the subgroup of patients who fulfilled the remission criteria, table 1 also presents the characteristics at the time of remission for both, the trial cohort (n=117) and the validation cohort (n=55). The distribution of the mSvdHS of the population is visualised as histogram in online supplementary figure S2.

Disease activity is strongly associated with physical function in a non-linear way

Longitudinal analysis showed a non-linear, significant association (p<0.001) of disease activity with physical function (visualised in online supplementary figure S1). Increases of disease activity at the low end of the disease activity scale affect physical function, and this effect attenuates with higher levels of disease activity in a non-linear way (quadratic association). Baseline characteristics of these patients were consistent with those of all patients included in the GO-REVEAL trial (data not shown).[22]

Structural damage leads to functional disability independent of disease activity

Table 2 summarises the estimates (95% CIs) and the p values for the different parameters in the GEE models for all patients (main analysis; adjusted for DAPSA), as well as in DAPSA remitters (without adjustment for disease activity). The model parameters (betas) correspond to the effects of each increment of the radiographic score on the HAQ scale. Given the large range of the mSvdHS in this cohort (0–218) and the small range of the HAQ (0–3), the HAQ increments in relation to damage are expected to be small. In the main analysis, significant effects on physical impairment were seen for the total mSvdHS (Figure 1, p=0.005). The subsequent analyses of subscores showed that this was mainly related to the effects of JSN (p=0.001) and to a lesser extent to the effects of ERO (p=0.019), as visualised in Figure 2A. Putting the estimate (β=0.002) of the remission model into clinical context, a patient in DAPSA remission with an mSvdHS of 10, 50, 100 or 150 would have a predicted 'residual' mean HAQ of 0.02, 0.1, 0.2 and 0.3, respectively. As the minimally clinical important difference of the HAQ in PsA lies between 0.3 and 0.35,[16 23] patients with long-standing PsA and/or substantial radiographic damage would experience a clinically meaningful irreversible change of physical function.

Table 1 Characteristics of patient populations. (A) Baseline characteristics of the total trial population and subgroups of the trial population and the validation cohort at first visit; (B) Patient characteristics at the time of remission for the trial population and the validation cohort

	(A) At baseline					(B) At remission	
	GO-REVEAL			Validation			
	All patients	Remission*	Major response†	All patients	Remission‡	GO-REVEAL	Validation
Number of patients	363	117	67	160	55	117	55
Female (%)	153 (42.1)	39 (33.3)	30 (44.8)	75 (46.8)	15 (27.3)	39 (33.3)	15 (27.3)
Age (years)	46.9±10.8	44±11.5	43.6±11.2	52.3±12	51.8±12.1	45.1±11.6	52.4±11.7
Disease duration (years)	7.4±7.4	7.2±6.7	7.8±8.3	2.9±7.1	3.6±8.7	8.1±6.7	7.2±8.9
Swollen joints (0–66)	13.3±10.3	11.1±8.3	17.1±11.7	2.7±3.5	2.3±3.4	0.3±0.6	0.4±0.7
Tender joints (0–68)	23.1±16.5	16.7±11.4	29.3±17.6	10.1±14.5	4.2±8.9	0.5±0.8	0.2±0.4
Pain (VAS 0–100)	55.9±23.5	48.7±26.1	66±21.2	41.2±26.1	22.1±20.3	4.6±4.6	7.4±7.4
Patient global (VAS 0–100)	53.2±23.3	46.9±24.6	63.9±21	44.8±27.4	26.9±22.8	4.7±4.9	8±7.3
Evaluator global (VAS 0–100)	54.5±17.9	49.9±16.9	59.8±17.2	13.3±13.9	8.8±11.4	5±9.5	1.6±2.8
CRP (mg/dL)	1.4±1.6	1.4±1.6	2.2±1.9	0.9±0.8	0.5±0.3	0.4±0.2	0.5±0.3
HAQ (0–3)	1±0.6	0.8±0.6	1.5±0.4	0.8±0.8	0.3±0.4	0.1±0.3	0.2±0.3
SF-36 PCS (0–100)	32.5±9.8	36±10	NA	NA	NA	51.4±6.5	NA
Total mSvdHS (0–528)§	9.5 (3; 26)	9.5 (3; 26)	12 (4; 56.2)	6 (2; 14)	8 (2; 21)	8.5 (3; 23)	8 (2; 21)
ERO Score (0–320)§	5.5 (2; 15.5)	6 (2; 16.5)	9 (2; 31)	0 (0; 1)	0 (0; 3)	5 (2; 16)	0 (0; 3)
Score JSN (0–208)§	3.5 (1; 10.5)	3 (0.5; 8.5)	4.5 (1; 17.5)	5 (2; 13)	7 (2; 16)	3 (0.5; 7.5)	7 (2; 16)
DAPSA score	48.8±26.3	38.9±21.7	61.6±29.1	NA	NA	2±1.2	NA
cDAPSA score	47.4±26.1	37.4±21.1	59.4±28.5	22±19.7	11±13.4	1.7±1.2	2.2±1.4

All values are presented as mean±SD except stated otherwise.
*DAPSA ≤4 at the time of remission.
†85% DAPSA improvement from baseline and HAQ baseline ≥1.
‡cDAPSA ≤4.
§Median (first quartile; third quartile).
cDAPSA, clinical Disease Activity Index for Psoriatic Arthritis Score (TJC68+SJC66+Patient Global (0–10)+Patient Pain (0–10)); CRP, C reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis Score (TJC68+SJC66+Patient Global (0–10)+Patient Pain (0–10)+CRP (mg/dL)); ERO, erosion; HAQ, Health assessment Questionnaire; JSN, joint space narrowing; mSvdHS, modified Sharp/van der Heijde Score; SF-36 PCS, 36-Item Short Form Survey—Physical Component Score; VAS, .

Table 2 Results from longitudinal analyses of the influence of structural damage on physical function (measured by the Health Assessment Questionnaire Disability Index (HAQ))

	All patients* (n=363)		Remission patients† (n=117)	
Parameter	**Estimate (95% CI)**	**p**	**Estimate (95% CI)**	**p**
Model 1 (effects of total modified Sharp/van der Heijde Score (mSvdHS))				
Intercept	0.24 (0.163 to 0.316)	<0.001	0.097 (0.025 to 0.168)	0.008
Visit	0.0002 (–0.0003 to 0.0008)	0.352	–0.0004 (–0.0011 to 0.0004)	0.312
DAPSA	0.022 (0.018 to 0.025)	<0.001	–	–
DAPSA²	–0.0001 (–0.0001 to -7.2×10^{-5})	<0.001	–	–
Total mSvdHS	**0.002 (0.001 to 0.003)**	**0.005**	**0.002 (0.0002 to 0.004)**	**0.029**
Model 2 (effects of erosion score (ERO))				
Intercept	0.246 (0.169 to 0.323)	<0.001	0.104 (0.032 to 0.176)	0.005
Visit	0.0002 (–0.0003 to 0.0008)	0.369	–0.0004 (–0.0012 to 0.0004)	0.297
DAPSA	0.022 (0.018 to 0.025)	<0.001	–	–
DAPSA²	–0.0001 (–0.0001 to -7.2×10^{-5})	<0.001	–	–
ERO score	**0.003 (0 to 0.005)**	**0.019**	**0.003 (0 to 0.005)**	**0.058**
Model 3 (effects of joint space narrowing score (JSN))				
Intercept	0.238 (0.163 to 0.314)	<0.001	0.092 (0.023 to 0.161)	0.009
Visit	0.0003 (–0.0003 to 0.0008)	0.348	–0.0004 (–0.0011 to 0.0004)	0.325
DAPSA	0.022 (0.018 to 0.025)	<0.001	–	–
DAPSA²	–0.0001 (–0.0001 to -7.3×10^{-5})	<0.001	–	–
JSN score	**0.005 (0.002 to 0.007)**	**0.001**	**0.005 (0.001 to 0.009)**	**0.010**

Estimates are presented as estimate of HAQ (95% lower CI to 95% upper CI).
*All visits of patients with available radiographic scoring.
†Visits in DAPSA remission (DAPSA ≤4) of patients with available radiographic scoring.
DAPSA, Disease Activity Index for Psoriatic Arthritis.

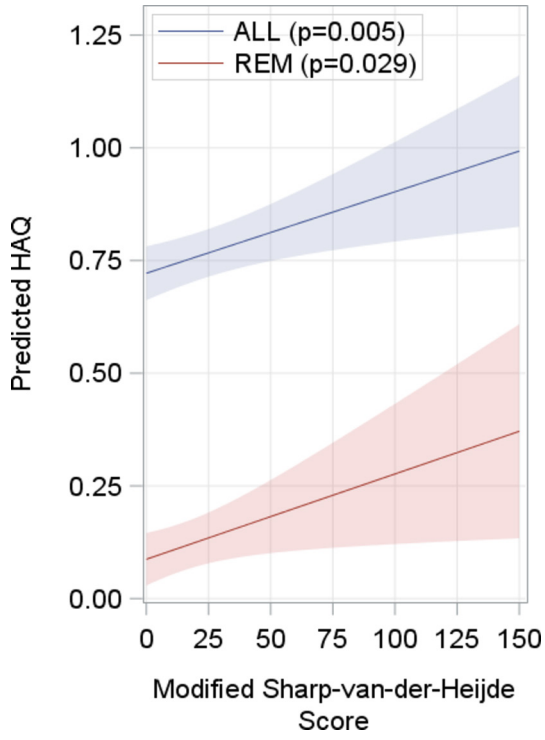

Figure 1 Predicted association of structural damage on physical function in patients with psoriatic arthritis, estimated for week 24. Blue curve: model in all patients (ALL, n=363), adjusted for Disease Activity Index for Psoriatic Arthritis (DAPSA) and estimated for for the mean DAPSA over all visits (DAPSA=25); red curve: model in all remission patients (REM, DAPSA≤4, n=117) without additional disease activity adjustment. Shaded areas represent the 95% CIs. HAQ, Health Assessment Questionnaire.

In the cohort achieving DAPSA remission, all radiographic changes were significantly related to HAQ scores (Figure 1 and Figure 2B).

Additionally, we investigated how other core disease activity variables are affected by damage and found no significant association besides the HAQ (see online supplementary table S4).

NNT to prevent irreversible functional impairment

At week 52, 44 of 60 patients (73.3%) achieving DAPSA LDA (DAPSA≤14) in the first (lowest) tertile of the mSvdHS normalised their HAQ (HAQ<0.5), while 29 of 54 (53.7%) of the third tertile achieved a normal HAQ. Comparing the first and third tertile, the RR of achieving a normal HAQ is 0.58 (95% CI 0.35 to 0.96, p=0.029). Thus, overall, the potential of achieving a normal HAQ is highly reduced in patients in the highest damage tertile. Further, patients achieving LDA in the first mSvdHS tertile have an ARR of 0.196 in HAQ normalisation. In a classical invention study, this risk reduction would correspond to an NNT of 5 (95% CI 2.7 to 42.4).

The mean disease duration was different between the first and third tertile achieving LDA at week 52 (5.15±5 and 11.3±9.1; p<0.001), as well as the mean age (40.5±8.7 and 49.4±11.5; p<0.001). While there were no differences in mean DAPSA at baseline, the mean HAQ scores at baseline were significantly lower in the first tertile, compared with the third (0.81±0.60 and 1.11±0.69, p=0.015).

Functional responsiveness is impaired in patients with structural damage

In the analysis of DAPSA major responders, the change of HAQ scores decreased significantly with increasing levels of overall structural damage (total mSvdHS; p=0.010 and p=0.013 for absolute or relative HAQ change, respectively) (table 3, figure 3). This was driven mainly by JSN and less by ERO (Figure 2C,D).

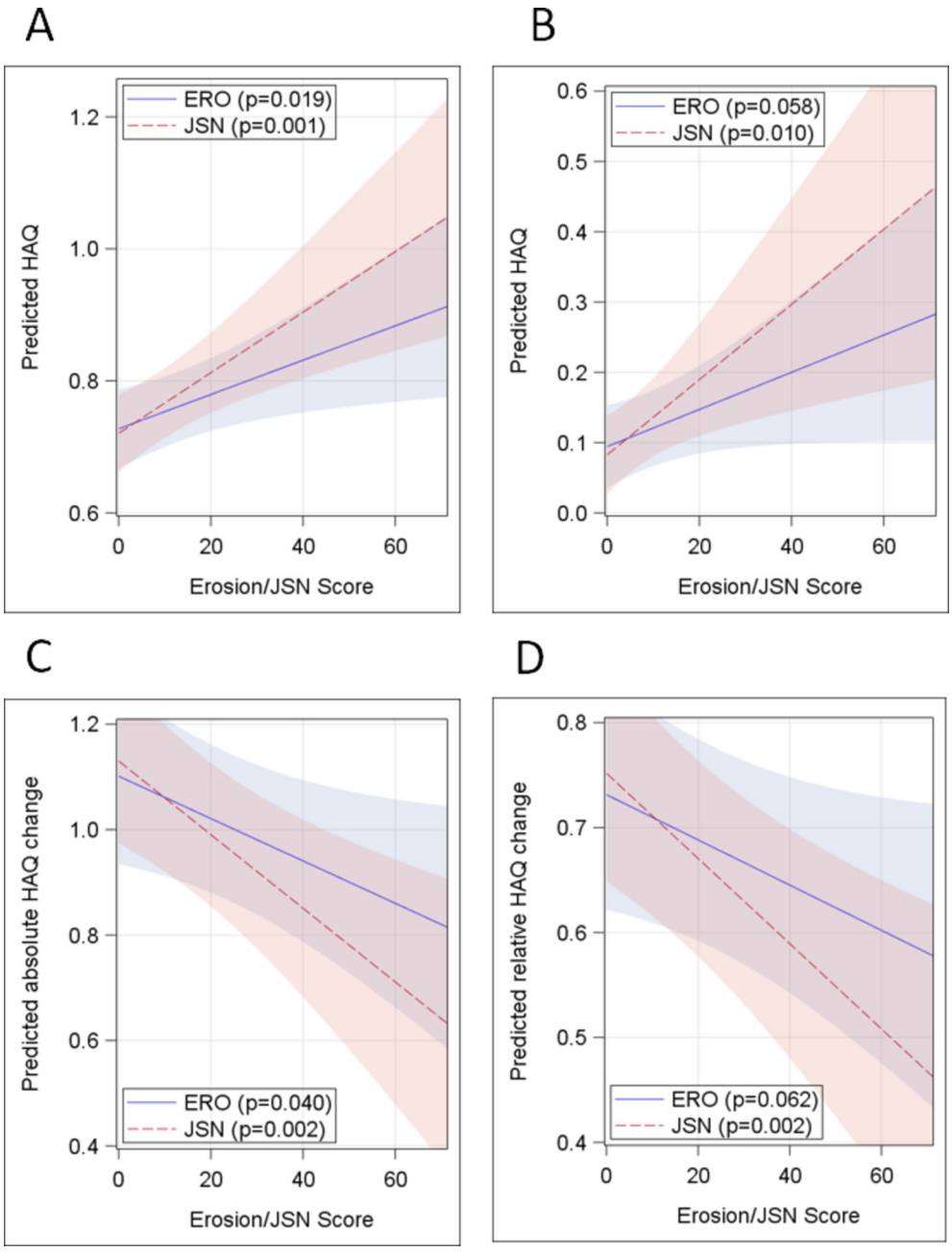

Figure 2 Predicted association of joint space narrowing (JSN) and erosion scores on physical function and functional responsiveness in patients with psoriatic arthritis, estimated for week 24. Red curves: JSN; blue curves: ERO score; (A) Predicted Health Assessment Questionnaire (HAQ) in all patients, adjusted for Disease Activity Index for Psoriatic Arthritis (DAPSA) and estimated for the mean DAPSA over all visits (DAPSA=25, n=363); (B) Predicted HAQ in all DAPSA remission patients (DAPSA ≤4) without adjustment for disease activity (n=117); (C) Predicted absolute HAQ change in patients with a baseline HAQ of ≥1 and a DAPSA major response (≥85% DAPSA improvement from baseline) (n=67), adjusted for baseline HAQ. (D) Predicted relative HAQ change in patients with a baseline HAQ of ≥1 and a DAPSA major response (≥85% DAPSA improvement from baseline) (n=67), adjusted for baseline HAQ. Shaded areas represent the 95% CIs.

Validation analyses using a different cohort and a different functional measure

The analyses including all patients and the remission analyses were validated in the clinical practice cohort, in which the significant association of HAQ with mSvdHS ($p<0.001$), JSN ($p<0.001$) and ERO ($p<0.001$) was confirmed. Additionally, we validated the remission as well as the responsiveness analyses using the SF-36 PCS instead of HAQ as outcome variable in GO-REVEAL patients (data provided as online supplementary material).

DISCUSSION

PsA is associated with significant disability. A major factor in this respect is disease activity, since especially pain, swelling and stiffness impair physical function.[17 24] In the present study, we show that disability increases with increasing PsA disease activity, as assessed by the DAPSA. Moreover, in line with similar reports,[3 8] we also observed a significant association of disability with joint damage, since HAQ scores increased with higher mSvdHS. However, here, we provide a numerical estimate for the irreversible disability associated with joint damage. Importantly, as joint damage in PsA relates to

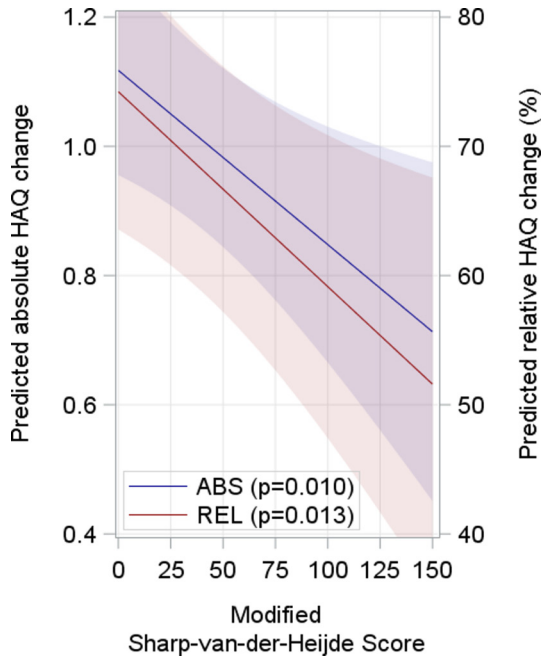

Figure 3 Predicted association of radiographic damage and functional responsiveness in patients with psoriatic arthritis. Analysis of patients with a baseline Health Assessment Questionnaire (HAQ) of ≥1 and a Disease Activity Index for Psoriatic Arthritis (DAPSA) major response (≥85% DAPSA improvement from baseline) (n=67), adjusted for baseline HAQ. Absolute (ABS) and relative (REL) HAQ changes at week 24 are shown for different levels of radiographic scores, and are estimated for patients with a baseline HAQ=1.5. Shaded areas represent the 95% CIs.

both, bony as well as cartilage changes, like in RA,[2 4–6] JSN as a surrogate of cartilage damage was more strongly associated with functional impairment than ERO. Therefore, also for PsA, a focus on preserving joint integrity can be called on, with a specific consideration of JSN in radiographic assessment. Other core set disease activity characteristics, including joint counts, patient global assessment, evaluator global assessment and pain, do not show associations with higher degrees of damage.

While the estimates of the models are small, they clearly cross the reported threshold of clinical meaningfulness of the HAQ if early, established and late PsA are considered. The association of disability with joint damage was particularly prominent when we focused on patients who were in clinical remission and whose physical function was, therefore, not affected by disease activity. As joint damage is presumed to be irreversible, so would also be the residual disability caused by joint damage. Greater amounts of damage, therefore, preclude patients with PsA to normalise physical function, even if their disease activity is optimally controlled. Thus, prevention of joint destruction from occurring and, especially, progressing constitutes a very important principle for the treatment of PsA.

With all these data at hand, the claim can be made that structural changes in PsA are not mere epiphenomena of the disease, but clearly relate to physical functioning and overall health status of these patients. On the other hand, however, the main result of our study also reveals that the responsiveness of the HAQ decreases with higher structural damage in patients achieving major treatment response. Physical function is a major outcome in patients with chronic musculoskeletal disease, such as PsA. For that reason, functional assessment is often included in composite disease activity and outcomes scores of PsA.[13] Since, as the present data reveal, impairment of physical function may be partly irreversible and thus will not normalise in the presence of significant joint damage, the inclusion of functional scores such as the HAQ in composite scores that measure the disease process may have to be revisited. Indeed, we have observed that similar effects as on the HAQ are seen when assessing the physical component subscale of the SF-36, which supports the fact that the concept is independent of the functional instrument used.

Our findings were initially derived from a clinical trial cohort. Patients in clinical trials may only partly reflect those seen in

Table 3 Impaired functional responsiveness in patients achieving major response of the Disease Activity Index for Psoriatic Arthritis (DAPSA; 85% improvement from baseline). Results of longitudinal analyses for absolute and relative change in physical function (measured by the Health Assessment Questionnaire Disability Index (HAQ))

	Absolute HAQ change* (n=67)		Relative HAQ change† (n=67)	
Parameter	**Estimate**	**p**	**Estimate**	**p**
Model 1 (effects of total modified Sharp/van der Heijde Score (mSvdHS))				
Intercept	−0.026 (−0.447 to 0.396)	0.905	0.759 (0.492 to 1.027)	<0.001
Baseline HAQ	0.747 (0.489 to 1.005)	<0.001	−0.023 (−0.168 to 0.122)	0.758
Visit	0.001 (−0.001 to 0.003)	0.338	0.001 (−0.001 to 0.002)	0.279
Total mSvdHS	**−0.003 (−0.005 to −0.001)**	**0.010**	**−0.002 (−0.003 to −0.0003)**	**0.013**
Model 2 (effects of erosion score (ERO))				
Intercept	−0.017 (−0.447 to 0.413)	0.937	0.764 (0.493 to 1.036)	<0.001
Baseline HAQ	0.73 (0.466 to 0.994)	<0.001	−0.034 (−0.181 to 0.114)	0.655
Visit	0.001 (−0.001 to 0.003)	0.308	0.001 (−0.001 to 0.002)	0.258
ERO score	**−0.004 (−0.008 to −0.0002)**	**0.040**	**−0.002 (−0.004 to 0.0001)**	**0.062**
Model 3 (effects of joint space narrowing score (JSN))				
Intercept	−0.038 (−0.449 to 0.372)	0.854	0.752 (0.49 to 1.014)	<0.001
Baseline HAQ	0.765 (0.512 to 1.019)	<0.001	−0.011 (−0.154 to 0.132)	0.882
Visit	0.001 (−0.001 to 0.003)	0.3A85	0.001 (−0.001 to 0.002)	0.314
JSN score	**−0.007 (−0.011 to −0.003)**	**0.002**	**−0.004 (−0.007 to −0.002)**	**0.002**

*Absolute HAQ change was defined as HAQ at baseline—HAQ at visit.
†Relative HAQ change was defined as (HAQ at baseline—HAQ at visit)/HAQ at baseline.

clinical practice. However, we were able to validate the initial observations in a cohort of patients from routine clinical care. Thus, the data obtained are pertinent for both, patients included in clinical trials as well as those seen in practice.

While our study reveals novel evidence regarding joint damage-induced irreversible disability in PsA, it may not provide the full spectrum of the complex interplay between disability and disease-related factors. Our study has several limitations: (1) We did not address comorbidities and psychological factors in the context of disability. Indeed, comorbidities have been shown to significantly impact irreversible disability in RA,[25] and this is also likely the case in PsA; however, we did not have data on comorbidities available in the cohorts studied. Also, skin involvement does not seem to affect physical function in PsA,[22] even if a PsA modified version of the HAQ is used.[26] (2) Non-pharmaceutical treatment, including physiotherapy, may also contribute to the improvement of physical function, even in patients with advanced radiographic damage. (3) We are mainly addressing physical function of PsA patients with oligoarticular or polyarticular peripheral joint disease, which is predominant in PsA,[27] but the mSvdHS does not take axial skeleton involvement into account and axial changes may also contribute to disability. Therefore, in patients who have only one or very few peripheral joints involved or predominantly axial disease, irreversible disability may be underestimated by using mSvdHS only. (4) Furthermore, bony proliferation is not included in the mSvdHS and may also contribute to loss of physical function. (5) Additionally, secondary osteoarthritis has not been taken into account. (6) Finally, most patients in the GO-REVEAL study had low degrees of structural damage (visualised in online supplementary figure S2), but we could still observe significant implications on functional outcomes. Nevertheless, extrapolation to values beyond the observed data may not be legitimate.

The data presented reveal that damage in PsA is associated with irreversible disability as in RA and that the major culprit in this respect is cartilage destruction. This implies that prevention of joint damage and especially preservation of cartilage structure is of particular importance and, therefore, would support the claim to diagnose and treat PsA rapidly and effectively, as well as the currently accepted treatment targets of remission of disease activity. Remission will best prevent joint damage progression,[28] and thus will also lead to best possible functional outcomes in PsA over time.

In conclusion, our results reveal that responsiveness of functional limitations decreases with increasing joint damage. They further suggest that—similar to what has been shown in RA—JSN is functionally more important than ERO. Both achievable HAQ levels and HAQ responses are negatively impacted by a high degree of structural damage. Consideration of these components is clinically and therapeutically relevant, as the HAQ component related to inflammation is expected to be reversible, while the component related to destructive changes is not.

Acknowledgements We thank Janssen for provision of a 90% random data cut of patients in the GO-REVEAL trial for our analyses. We thank Gabriela Supp for radiographic scoring of all radiographic images of the validation cohort used in this study.

Contributors Study design: AK, JSS, DA. Data acquisition: DB. Data analysis: AK, JSS, DA. Manuscript writing: AK, DB, JSS, DA.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data were partly provided by Janssen, who did not provide any funding for the study.

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Ann Rheum Dis published online August 23, 2017