was based on patient opinion. ROC curve was constructed to examine the optimum cut-off for disease flare. Agreement between the FLARE instrument and patient opinion was assessed by Cohen’s kappa. Test-retest was assessed in 28 patients with stable disease who underwent repeat assessment within 2 weeks and evaluated by intra-class correlation coefficient (ICC).

**Results:** The FLARE questionnaire was administered at 367 patient encounters. ROC analysis indicated that the optimum cut-off for a flare of disease was 4 (sensitivity 82%, specificity 76%; area under curve 0.85: figure). Mean PASDAS scores were 2.7 and 6.3 for no-flare (4) and flare (≥4) respectively (p < 0.0001).

For those patients who were having a flare the frequency of response to each question is given in the table. Agreement between patient opinion and questionnaire was 0.57, and between patient opinion and physician (based on treatment escalation) 0.43. ICC for the questionnaire was 0.87 (95% CI 0.72 – 0.94).

**Conclusion:** In PsD a flare represents escalation of symptoms and signs across multiple domains, as measured by the FLARE instrument; a score of 4 or more has external validity both in terms of composite disease activity and overall patient opinion of the state of their condition.

**References:**


### Table

<table>
<thead>
<tr>
<th>Item</th>
<th>FLARE instrument score ≤4</th>
<th>FLARE instrument score ≥4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening itch</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Worsening skin area</td>
<td>35 (19)</td>
<td>108 (58)</td>
</tr>
<tr>
<td>Increasing joint pain</td>
<td>27 (15)</td>
<td>91 (49)</td>
</tr>
<tr>
<td>Increasing number of tender joints</td>
<td>34 (19)</td>
<td>161 (86)</td>
</tr>
<tr>
<td>Decrease in ability to perform activities</td>
<td>20 (11)</td>
<td>142 (76)</td>
</tr>
<tr>
<td>Worsening in ability to move easily</td>
<td>8 (4)</td>
<td>126 (67)</td>
</tr>
<tr>
<td>Increase in frustration</td>
<td>14 (8)</td>
<td>142 (76)</td>
</tr>
<tr>
<td>Worsening in depression</td>
<td>8 (4)</td>
<td>90 (48)</td>
</tr>
<tr>
<td>Worsening in feeling of tiredness all the time</td>
<td>37 (21)</td>
<td>148 (79)</td>
</tr>
<tr>
<td>Worsening in the number or combination of symptoms</td>
<td>7 (4)</td>
<td>134 (72)</td>
</tr>
</tbody>
</table>

*from your disease*

**Figure.** ROC analysis of FLARE questionnaire

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**AB1242**

**A NOVEL BIOMARKER OF MMP-CLEAVED PROLARGIN IS ELEVATED IN PATIENTS WITH PSORIATIC ARTHRITIS COMPARED TO OTHER FIBRO-INFLAMMATORY DISEASES**

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**Background:** Psoriatic Arthritis (PsA) is a chronic inflammatory disease, characterized by involvement of skin, axial and peripheral skeleton. Prolargin is a class III small leucine-rich proteoglycan found to be expressed in connective tissues of patients with PsA, and previously suggested to be remodelled upon treatment. Fragments of prolargin could quantitatively tissue turnover in individuals with PsA and reflect pathological tissue changes in these patients.

**Objectives:** This study aimed at developing an immunoassay targeting a neo-epitope of prolargin cleaved by matrix metalloproteinases (MMPs), named PROM; and measure PROM levels in serum from two cohorts of patients affected by PsA and healthy controls.

**Methods:** Development of a novel immunoassay targeting a specific MMP-generated neo-epitope fragment of prolargin (PROM) together with technical validation was performed, and then evaluated in serum from two independent cohorts. The technical validation included inter- and intra-variation, linearity, spiking recovery, stability and specificity. Specificity was tested using an elongated peptide, a truncated peptide and a non-sense peptide. The Discovery Cohort consists of 13 healthy individuals and 11 PsA patients, mean age 58, 60.3% female and 100% caucasian. The Validation Cohort included 35 healthy individuals and 112 PsA patients with low disease activity included in a 24-week randomized, double-blind, placebo-controlled trial of 3g n-3 polyunsaturated fatty acids (PUFA), a cohort of patients diagnosed with PsA by the CASPAR criteria. These patients had a mean age of 50.8, 57.8 % female and 100 % caucasian. Clinical variables and serum samples were collected at baseline and after 24 weeks of follow-up. An unpaired t-test was used for evaluation of healthy individuals and patients affected by PsA, while a paired t-test was used for evaluation of treatment at baseline and after 24 weeks.

**Results:** A technically robust and specific assay was developed. The inter- and intra-assay variation of PROM was determined as 14% and 4 % respectively. PROM showed a good dilution recovery, spiking recovery, and storage/freeze-thaw stability (All, 100%±20%). PROM showed to be specific towards the targeted sequence, and did not show any reactivity towards the truncated peptide, elongated peptide or non-sense peptide. In the Discovery Cohort, serum levels of PROM were increased in patients with PsA compared to healthy individuals (p=0.032, Figure 1A). This increase was confirmed by the Validation Cohort, where PsA patients were significantly increased compared to healthy individuals at baseline (p=0.002, Figure 1B).

After 24 weeks, the levels of PROM were unchanged in the n-3 PUFA treated group.

**Figure 1.**

**Conclusion:** The novel biomarker PROM, reflecting connective tissue remodelling, is elevated in PsA patients compared to healthy controls in two independent cohorts. No significant association was found for PROM in a low disease activity group of PsA patients treated with n-3 PUFA.

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AB1243
TRAINING AND VALIDATION OF A MULTIVARIATE PREDICTOR OF RISK OF RADIOGRAPHIC PROGRESSION FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The multi-biomarker disease activity (MBDA) score, adjusted for age, sex and adiposity (MBDAadj), has been shown to be better than several conventional disease activity measures for predicting risk for radiographic progression (RP) in patients with rheumatoid arthritis (RA).1 Serologic status and other non-disease activity measures are also predictive of RP risk. Combining them with the MBDAadj should result in a stronger prognostic test for RP than any one measure alone.

Objectives: Develop a multivariate model for predicting risk for RP that includes the adjusted MBDA score and other known predictors of RP.

Methods: Four RA cohorts were used, two for training (OPERA and BRASS, n=555) and two for validation (SWEFOT and Leiden, n=397). Each pair of cohorts was heterogeneous in disease duration and treatment history. BMI data were not available for one validation cohort, so a BMI surrogate was modeled using forward selection with the training cohorts and 3 others (CERTAIN, InfMount, HACER) (N=1411). An RP risk score was then trained using forward selection in a linear mixed-effects regression, considering disease-related and demographic variables as predictors of change in modified total Sharp score over one year (ΔmTSS), with a random effect on cohort. The RP risk score was validated as a predictor of RP with two cutoffs (ΔmTSS >3 and >5) using logistic mixed-effects regression. Odds ratios (OR) and 95% profile likelihood-based confidence intervals (CI) were calculated from the models and significance was assessed by likelihood ratio tests. Risk ratios (OR) and 95% profile likelihood-based confidence intervals (CI) were calculated from the models and significance was assessed by likelihood ratio tests.

Results: The BMI surrogate included leptin, sex, age and age2 and correlated well with BMI (p = 0.76). In training, the most significant independent predictors of RP were MBDAadj (p = 0.00020), seropositivity (p = 9.3 x 10-5) and BMI surrogate score (p = 0.013) and use of targeted therapy (p = 0.0026). The final model was: RP risk score = 0.024 x MBDAadj + 0.093 if seropositive – 0.063 x BMI surrogate score (p = 0.013) and use of targeted therapy (p = 0.0026). The final model was: RP risk score = 0.024 x MBDAadj + 0.093 if seropositive – 0.063 x BMI surrogate score – 0.61 if using a targeted therapy. In validation, the OR (95% CI) of the RP risk score for patients with mTSS >3 or >5 were 2.2 (1.6, 3.2) (p = 2.6 x 10-6) and 3.1 (2.0, 5.0) (p = 5.7 x 10-8), respectively (Figure 1). The odds of a patient having RP were MBDAadj (p = 0.00020), seropositivity (p = 9.3 x 10-5), BMI surrogate = 0.76). In training, the most significant independent predictors of RP were MBDAadj (p = 0.00020), seropositivity (p = 9.3 x 10-5), BMI surrogate score (p = 0.013) and use of targeted therapy (p = 0.0026). The final model was:

Conclusion: A multivariate model containing adjusted MBDA score, seropositivity, a BMI surrogate and use of targeted therapy has been trained and validated as a prognostic test for radiographic progression in RA.

References:

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AB1244
PROGNOSTIC FACTORS IN IGG4-RELATED DISEASE: A LONG-TERM MONOCENTRIC CHINESE COHORT STUDY

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Background: Through initial response to treatment with GC, the patients with IgG4-related disease (IgG4-RD) exhibited high relapse rate after reduction or withdrawal of GC treatment, indicated the unsatisfactory prognosis for IgG4-RD. It is of clinical significance to develop new informative risk factors for refractory and relapsed disease.

Objectives: To evaluate the prognosis of IgG4-RD and identify predictive factors for treatment resistance and disease relapse in a Chinese cohort.

Methods: 102 patients newly diagnosed with IgG4-RD were followed for 6-111 months. Clinical data were compared between patients whose disease went into remission and those who suffered refractory or relapsed disease. Predictive factors for refractory and relapsed disease were calculated by univariate analysis.

Results: Among the 78 patients who received medical treatment with regular follow-up, 55 (59.8%) patients sustained clinical remission, and 23 (25%) patients suffered refractory or relapsed disease. The mortality and incidence of malignancy were both 4.35% during follow-up. Serum TNF-α ≥ 13 pg/ml, sIL-2R ≥ 1010 pg/ml, TC < 3.55 mmol/L, LDL < 2.0 mmol/L, IgG > 20.2 g/L, GC withdrawal, and treatment without immunosuppresser (IM) during the maintenance period (OR 3.23) were predictive factors for refractory and relapsed IgG4-RD. The combination of GC and IM treatment was protective (OR 0.338) against refractory and relapsed IgG4-RD.

Conclusion: Serum TNF-α, sIL-2R, LDL, TC, IgG, GC withdrawal, and treatment without IM during the maintenance period were predictive factors for refractory and relapsed IgG4-RD. Treatment with GC and IM may protect against refractory and relapsed IgG4-RD.

References: