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Validity of a 2-component imaging-derived disease activity score (2C-DAS28) for improved assessment of synovitis in early rheumatoid arthritis

Elizabeth M.A. Hensor^{1,2}, Paul McKeigue³, Maya H. Buch^{1,2}, Jennifer H. Barrett^{2,4}, Jackie L. Nam^{1,2}, Jane Freeston^{1,2,5}, Marco Colombo³, Athina Spiliopoulou^{3,6}, Felix Agakov⁶, Stephen Kelly⁷, Myles J. Lewis⁷, Stephanie F. Ling⁸, Sebastien Viatte⁸, Suzanne MM Verstappen^{9,10}, Anne Barton^{8,10}, Alexander J. MacGregor¹¹, Costantino Pitzalis⁷, Paul Emery^{1,2}, MATURA consortium, IACON Consortium, PEAC Consortium, Philip G. Conaghan^{1,2}, Ann W. Morgan^{1,2}

- 1. Leeds Institute of Rheumatic and Musculoskeletal Medicine, School of Medicine, University of Leeds, UK
- 2. NIHR-Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, UK
- 3. Usher Institute for Population Health Sciences and Informatics, University of Edinburgh, UK
- 4. Leeds Institute of Cancer and Pathology, School of Medicine, University of Leeds, UK
- 5. Leeds Teaching Hospitals NHS Trust, Leeds, UK
- 6. Pharmatics Limited, Edinburgh, UK
- 7. Barts and the London School of Medicine and Dentistry, William Harvey Research Institute, Queen Mary University of London
- 8. Arthritis Research UK Centre for Genetics and Genomics, Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, UK
- 9. Arthritis Research UK Centre for Epidemiology, Division of Musculoskeletal and Dermatological Sciences, The University of Manchester, UK
- 10. NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, UK
- 11. Norwich Medical School, University of East Anglia, Norwich, UK

Background

Imaging of joint inflammation provides a standard against which to derive an updated disease activity score (DAS) for rheumatoid arthritis (RA). The objective of this study was to develop and validate a DAS based on reweighting the components of the DAS28 to maximize association with ultrasound-assessed synovitis.

Methods

Early RA patients from 2 observational cohorts (Leeds Inflammatory Arthritis Continuum (IACON) n=434 & Pathobiology of Early Arthritis Cohort (PEAC) n=117), and a clinical trial (Infliximab as Induction Therapy in Early Rheumatoid Arthritis (IDEA) n=69) were assessed at intervals up to 104 weeks from baseline; all ultrasound scans were within 1 week of clinical exam. There were 899, 179 and 183 visits in each cohort. Associations of combined ultrasound grey scale and power Doppler scores (GSPD) with 28 tender and 28 swollen joint counts (TJC28 & SJC28), C-reactive protein (CRP, mg/L), erythrocyte sedimentation rate (ESR, mm/hr), general health visual analogue scale (mm) were examined in linear mixed model regressions. Cross-validation evaluated model predictive ability; coefficients learned from training data defined a re-weighted DAS28 which was validated against radiographic progression in an independent dataset (Norfolk Arthritis Register (NOAR) n=717 patients; 3037 observations) using generalised linear latent and mixed modelling (GLLAMM) for Larsen score and generalised estimating equations (GEE) for presence of erosion.

Results

Of the conventional DAS28 components only SJC28 and CRP were associated with GSPD in all three development cohorts. A 2-component model including SJC28 and CRP performed comparably to a 4-component model (R-squared 0.235, 0.392, 0.380 vs. 0.232, 0.380, 0.375 respectively). The re-weighted 2-component DAS28CRP outperformed the conventional DAS28 definitions (3C or 4C) in predicting GSPD (all \(\Delta\) test log-likelihood<-2.6, p<0.01). The new 2C-DAS28CRP was more strongly associated with Larsen score than conventional 3C-DAS28CRP and was also associated with erosions, whereas conventional 3C-DAS28CRP was not (Table 1).

Conclusion

A score based on SJC28 and CRP alone demonstrated stronger associations with synovitis and radiographic progression than the original DAS28 and should be considered in research on pathophysiological manifestations of early RA. The implications for clinical management of RA remain to be established.

Table 1: Associations between radiographic damage and conventional vs re-weighted DAS28CRP

Larsen score				
Model	β-coefficient (95% CI)	p-value	AIC	BIC
Conventional 3C DAS28CRP	0.78 (0.27, 1.30)	0.003	8140.085	8213.550
Re-weighted 2C DAS28CRP	1.15 (0.69, 1.61)	8.68E-07	8124.842	8198.308
Erosions				
Model	β-coefficient (95% CI)	p-value	QIC	
Conventional 3C DAS28CRP	0.07 (-0.03, 0.17)	0.174	1611.693	
Re-weighted 2C DAS28CRP	0.24 (0.15, 0.33)	2.02E-07	1545.371	

A(B)IC=Akaike (Bayesian) Information Criteria; 2(3)C=two (three) component; QIC=quasi-AIC