Background: The multi-biomarker disease activity (MBDA) score, adjusted for age, sex and adiposity (MBDA_adj), 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). Serologic status and other non-disease activity measures are also predictive of RP risk. Combining them with the MBDA_adj 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, InFoRM, RACER) available for one validation cohort, so a BMI surrogate was modeled using forward selection with the training cohorts and 3 others (CERTAIN, InFoRM, RACER) available for one validation cohort, so a BMI surrogate was modeled using forward selection with the training cohorts and 3 others (CERTAIN, InFoRM, RACER) available for one validation cohort. 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 (\(\Delta mTSS\)), with a random effect on cohort. The RP risk score was validated as a predictor of RP with two cutoffs (\(\Delta mTSS >3\) and \(\Delta mTSS >5\)) 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 curves were generated to show probability of RP as a function of the RP risk score.

Results: The BMI surrogate included leptin, sex, age and age^2 and correlated 0.36 with the adjusted MBDA score. For each unit increase in the adjusted MBDA score, there was a 0.61 risk reduction in RP. The final model was: \(\Delta mTSS >3\) or \(\Delta mTSS >5\), respectively.

Conclusions: 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: