CLINICAL SUMMARY

The Vectra® Score Adjusted for Age, Gender and Adiposity is Unsurpassed in Predicting Radiographic Progression

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Adjustment of the multi-biomarker disease activity score to account for age, sex, and adiposity in patients with rheumatoid arthritis

Curtis JR, et al. Oxford Academic, Rheumatology, 2018: December 24.

Objective: To develop and evaluate an adjusted score for the multi-biomarker disease activity (MBDA) test to account for the effects of age, sex and adiposity in patients with RA.

Baseline & Methods:

Three cohorts were used: Baseline demographic characteristics and data availability for the healthy normal cohort (n=318); RA clinical trial/registry cohort (Corrona-CERTAIN, InFoRM, RACER, OPERA, BRASS n=1411); commercial RA cohort (n=325,781)

Leptin as a proxy for body mass index in RA: Leptin showed a significant positive correlation with BMI in patients with RA and therefore serum leptin concentration was used as a proxy for adiposity.

Two models were developed to adjust MBDA for age, sex and adiposity, using either serum leptin concentrations or BMI as proxies for adiposity. Two cohorts were studied: 325,781 RA patients who had undergone MBDA testing and had age, sex and serum leptin concentrations (used for both models). And a cohort of 1411 patients from five studies/registries with BMI data was used only for the BMI-adjusted MBDA score.

Univariate and multivariate linear regression analyses evaluated the adjusted MBDA scores and conventional clinical measures as predictors of radiographic progression, assessed in terms of modified total Sharp score (ΔmTSS).

Results

Two models were developed, based on findings that MBDA score was higher in females than males and increased with age, leptin concentrations and BMI. In pairwise regression analyses, the leptin-adjusted (*P*=0.00066) and BMI-adjusted (*P*=0.0027) MBDA scores were significant independent predictors of ΔmTSS after adjusting for DAS28-CRP, whereas DAS28-CRP was not, after adjusting for leptin-adjusted (*P*=0.74) or BMI-adjusted (*P*=0.87) MBDA score. Moreover, the leptin-adjusted MBDA score was a significant predictor of ΔmTSS after adjusting for the BMI-adjusted MBDA score (*P*=0.025) or the original MBDA score (*P*=0.027), whereas the opposite was not true.

Radiographic progression: The measure with the numerically strongest association with radiographic progression was the leptin-adjusted MBDA score.

Association with DAS28* (DAS28 with no CRP or ESR component): The leptin-adjusted MBDA score was significantly associated with DAS28*

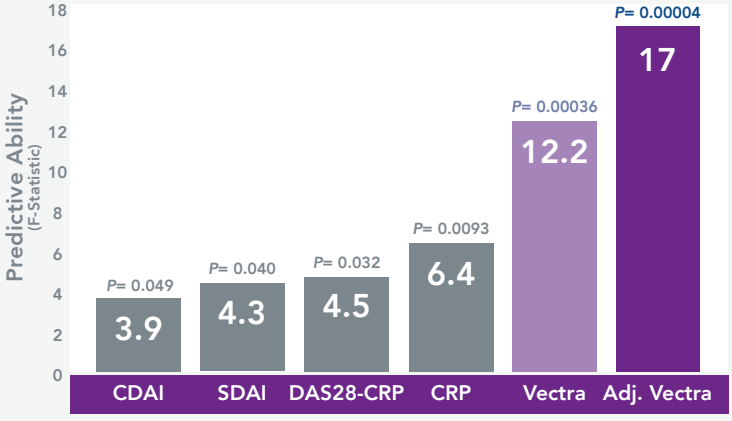
Association of disease activity measures with radiographic progression: The strongest association with radiographic progression was for the leptin-adjusted MBDA (17.0) (see Table 1)

Using pairwise linear regression models to test the ability of a measure to predict ΔmTSS independently of other measures:

- Leptin-adjusted (*P*= 0.00066) and BMI-adjusted (*P*= 0.0027) MBDA scores were statistically significant predictors of radiographic progression after adjusting for DAS28-CRP.
- Leptin-adjusted MBDA score predicted progression after adjusting for the original MBDA score (*P*= 0.027) or the BMI-adjusted MBDA score (0.025), whereas neither the original MBDA score nor the BMI-adjusted MBDA score predicted progression after adjusting for the leptin-adjusted MBDA score (*P*= 0.34 and *P*= 0.11, respectively).

Leptin-adjusted MBDA score had a statistically significant stronger and independent correlation with radiographic progression compared with the original MBDA score and the BMI-adjusted MBDA score.

The adjusted MBDA score significantly improves ability to predict clinical disease activity and radiographic progression.[1]



Conclusions: Leptin-adjusted MBDA score significantly adds information to DAS28-CRP and the original MBDA score in predicting radiographic progression. It may offer improved clinical utility for personalized management of RA.

Commercial and Clinical Applications:

- Vectra has developed an adjusted MBDA score for use in RA patients.
- The adjusted MBDA score has superior performance vs. the original MBDA score for RA patients.
- The adjusted MBDA score significantly improves ability to predict clinical disease activity and radiographic progression.
- Leptin-adjusted MBDA score had a statistically significantly stronger and independent correlation with radiographic progression, compared with the original MBDA score or the BMI-adjusted MBDA score.
- Leptin-adjusted MBDA has significantly improved ability to predict clinical disease activity and radiographic progression, as assessed by DAS28* and mTSS, respectively. These results suggest that the leptin-adjusted MBDA score represents an improvement over both the original MBDA score and commonly used disease activity measures for predicting radiographic progression in RA.

TABLE 1 Association of disease activity measures with radiographic progression

Variable	N°	Coefficient	F-statistic	P-value
Leptin-adjusted MBDA score	555	0.024 (0.012, 0.035)	17.0	0.000042
Seropositive (RF &/or anti-CCP)	Score	0.93 (0.46, 1.41)	14.8	0.00013
BMI-adjusted MBDA score	555	0.022 (0.011, 0.033)	14.4	0.00016
Original MBDA score	555	0.021 (0.009, 0.032)	12.9	0.00036
BMI	555	-0.071 (-0.11, -0.03)	10.9	0.0010
$\log_{10}$(CRP)	555	0.41 (0.10, 0.72)	6.8	0.0093
Baseline mTSSw	555	0.0033 (0.0005, 0.0062)	5.3	0.022
$\log_2$(Disease Duration + 1)	401	0.16 (0.016, 0.30)	4.8	0.030
DAS28-CRP	536	0.14 (0.012, 0.28)	4.6	0.032
SDAI	533	0.013 (0.001, 0.025)	4.3	0.040
CDAI	533	0.013 (0.000, 0.026)	3.9	0.049
DAS28*	536	0.014 (-0.02, 0.29)	3.1	0.079
Male	123/478	-0.31 (-0.80, 0.19)	1.5	0.23
Smoking Status - Never	240/478	Reference	0.79	0.46
Smoking Status - Former	160/478	0.22 (-0.27, 1.03)		
Smoking Status - Current	78/478	0.38 (-0.29, 0.73)		
Age	555	0.0025 (-0.013, 0.018)	0.09	0.76

Univariate linear regression was used to evaluate the association of baseline demographic and disease-related variables with ΔmTSS (degree of radiographic progression) in the combined OPERA and BRASS cohorts. Results are in descending order of statistical significance. [a]Patients within the total group that had suitable radiographic data (n=555) for whom baseline data were available for the indicated variable. Ratios indicate the number of patients in the indicated category and the total number with data available for that variable. [b]Coeffecients for continuous variable (i.e. all except seropositivity, male and smoking status) represent slope of the linear regression line, expressed as units of ΔmTSS per one-unit change in the indicated variable. anti-CCP: anti-cyclic citrullinated peptide; DAS28*: DAS28 with no CRP or ESR component; MBDA: multi-biomarker disease activity; ΔmTSS: change in modified total Sharp score.

1. How F-Statistic is Used: F-Statistic is a quantitative measure of how a model (with one or multiple variables) predicts an outcome. In this case, the F-Statistic quantifies how well Vectra predicts radiographic progression (RP). A ratio tells you how much of the variance in an outcome is explained by a model: Outcome=radiographic progression / Models=CRP, DAS28-CRP, Vectra, Adjusted Vectra, etc. The higher the F-Statistic, the better the predictive ability is.

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