FRI0036

VALIDATION OF RISK SCORES FOR PREDICTING PROGRESSION IN INDIVIDUALS "AT RISK OF RHEUMATOID ARTHRITIS"

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Background: Composite scores for risk of progression were described in 2015 in a cohort of 100 anti-cyclic citrullinated peptide (anti-CCP) + individuals at risk of developing Inflammatory Arthritis (IA) (1). The first score, designed for primary care, was based on anti-CCP and rheumatoid factor (RF) titres, small joints tenderness and early morning stiffness (EMS). A second score developed for secondary care added power Doppler presence (PD+) and/or at least one allele positive for the shared epitope (SE+).

Objectives: To validate previous data by scoring risk factors in a new cohort of 394 individuals.

Methods: Individuals at risk of developing IA selected by a positive anti-CCP test and a new musculoskeletal symptom have been followed in a single-centre prospective observational cohort since 2008. The previous risk score was derived from 100 patients. With the same recruitment and follow-up pathways, the next 394 consecutive participants were studied (full data were available for 373 patients for secondary care model). Participants followed for less than 10 weeks without progression were excluded.

Results: Participants from both cohorts were similar in terms of age and sex. Although the mean time to progression is comparable, there were significantly more participants with a high titre anti-CCP test in the 2015 cohort (Table 1).

Table 1. Patients characteristics

Score	2015	2020
N	100	394
Percentage of progression n/N	50/100 (50%)	82/413 (19.9%)
Mean of follow-up before progression to IA (Months (SD))	15.35 (15.27)	13.50 (12.62)
Mean follow-up of non progressors (Months (SD))	39.7 (15.82)	27.6 (19.75)
Mean follow-up duration: all participants (Months (SD))	27.7(19.36)	24.8 (19.38)
High CCP titre	83%	65%
Women	72%	72%
Smoker ever	72%	50%
Age (Mean (SD))	51.2 (11.9)	50.2 (13.474)

Cox multivariable analysis showed similar Hazard Ratios (HR) of progression in both groups (Table 2) confirming the high predictive value of high CCP/RF titre, early morning stiffness duration, power doppler presence and shared epitope. High risk of progression individuals identified by the secondary score were eight times more likely to develop IA (HR = 8.290, CI = 3.763-18.264, p<0.001), 50% of them had progressed at 2 years (Figure 1).

Table 2. Multivariable Cox regression analysis of time to progression to inflammatory arthritis.

	2015 (n=98)			2020 (n=394)		
	HR	p-value	CI	HR	p-value	CI
Primary care model						
High anti-CCP or RF titre	4.86	0.031	1.16–20.43	4.96	<0.001	1.445–3.526
EMS≥30min	1.86	0.039	1.03–3.37	2.26	<0.001	1.445–3.526
Small Joints Tenderness	1.42	0.252	0.78–2.57	1.30	0.249	0.832–2.035
Secondary care model						
High anti-CCP or RF titre	3.04	0.147	0.68–13.6	3.92	0.001	1.790–8.567
EMS≥30min	1.56	0.167	0.83–2.92	2.10	0.002	1.314–3.357
Small Joints Tenderness	1.54	0.178	0.82–2.88	1.34	0.216	0.843–2.135
PD signal	1.92	0.033	1.06–3.50	2.35	0.001	1.424–3.887
Shared epitope	1.57	0.272	0.70–3.49	2.33	0.003	1.333–4.059

Conclusion: These data from a new large cohort confirm the validity previous Leeds Risk Scores for Primary and Secondary care, and the fidelity of the risk factors over time to predict progression.

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Figure 1. Probability of IA free survival according to categories of risk in the secondary care model.

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FRI0037

ALL-CAUSE MORTALITY IN EARLY RHEUMATOID ARTHRITIS PREDICTED BY HEALTH ASSESSMENT QUESTIONNAIRE AT ONE YEAR

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Background: Patients with RA are at greater risk of mortality than the general population. Higher HAQ disability has been associated with hospitalizations and mortality in established RA; whether HAQ disability predicts mortality in early RA (ERA) is unknown.

Objectives: The objective of this study is to analyze how well the HAQ can predict future mortality in patients with early RA.

Methods: Data were from adult early RA patients (symptoms <1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) between 2007 and 2017; who initiated treatment with 1 or more DMARDs and had completed HAQ data at baseline and 1 year. Descriptive statistics, t-tests and chi-square tests were used to summarize and compare baseline patient characteristics including sociodemographic variables, RA characteristics and comorbidities amongst deceased and non-deceased patients. Discrete-time proportional hazards models were used to estimate crude and multi-adjusted associations between HAQ at baseline and 1 year, respectively, with all-cause mortality in each year of follow up.

Results: This study included 1724 patients with early RA; mean age was 55 years and 72% were female. In 10 years of follow up, 62 deaths (2.4%) occurred. Deceased patients had higher HAQ scores and DAS28 scores at baseline and at 1 year versus the non-deceased group. Age, male sex, lower education, smoking, more comorbidities, higher baseline disease activity and steroid use were associated with mortality in unadjusted survival models (Table 1). Contrary to HAQ at baseline, the association between all-cause mortality and HAQ at 1 year

remained significant even after adjusting for age, gender, comorbidities, disease activity, smoking, education, seropositivity, symptom duration and steroid use in adjusted survival models (Table 2).

Table 1. Unadjusted survival model: Association of each variable with all-cause mortality

Baseline Variable	Unadjusted Hazard OR	95% CI
Socio-Demographic		
Age (years)	1.10	1.07 – 1.13
Female	0.37	0.22 – 0.62
Caucasian (white or European)	1.01	0.46 – 2.24
Aboriginal	1.71	0.61 – 4.76
Education > high school degree	0.48	0.28 – 0.82
Current Smoker	1.81	1.01 – 3.24
Rheumatic Disease Comorbidity Index (0-9)	1.60	1.36 – 1.87
RA Characteristics		
Symptom duration (months)	0.99	0.91 – 1.08
Seropositivity in first year	1.11	0.55 – 2.23
DAS28 ESR or CRP if ESR is missing	1.26	1.06 – 1.51
Oral Steroid use	1.75	1.03 – 2.98

Table 2. Multivariable discrete-time survival models: HAQ baseline vs 1 year

Model	Model 1: Crude (Time + HAQ-DI)	Model 2: Adjusted for age + sex	Model 3: Adjusted for Model 2 + DAS28 + RDCI	Model 4: Adjusted for Model 3 + edu- cation, smoking, seropositivity, symptom duration and oral steroids use	Model 5: Adjusted for Model 3 + smoking, symptom duration only
HAQ-DI (0-3) (at baseline)	1.46 – 2.09	1.02 – 1.95	1.37 – 1.94	0.81 – 1.94	1.30 – 2.04
HAQ-DI (0-3) (at 1 year)	2.58 – 3.72	1.78 – 3.52	2.40 – 2.77	1.10 – 3.02	1.73 – 2.74

*Hazard OR, 95% CI

~HAQ-DI: (Health Assessment Questionnaire Disability Index); RDCI: Rheumatic Disease Comorbidity Index; DAS28: Disease Activity Score

Conclusion: Higher HAQ at 1 year was significantly associated with all-cause mortality in a large early RA cohort suggesting that poorer disease control and function in the first year of RA contributes to higher mortality.

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THE RELATIONSHIP BETWEEN ABATACEPT EXPOSURE AND EFFICACY MEASURES IN EARLY MTX-NAIVE ANTI-CITRULLINATED PROTEIN ANTIBODY-POSITIVE PATIENTS WITH RA DURING THE DE-ESCALATION PERIOD OF A PHASE IIIB STUDY

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Background: Although EULAR/ACR guidelines suggest tapering biologic treatment for RA following sustained remission in patients (pts), specific de-escalation (DE) regimens are not defined. The Phase IIIB Assessing Very Early Rheumatoid arthritis Treatment (AVERT)-2 trial (NCT02504268) is evaluating SC abatacept (ABA) + MTX versus ABA placebo (PBO) + MTX in Anti-Citrullinated Protein Antibody (ACPA)-positive pts with early (ACR/EULAR 2010 criteria; disease duration ≤6 mths), active RA (SDAI >11). AVERT-2 was designed to investigate achievement of SDAI remission and a clinically meaningful dose DE strategy among pts in sustained remission who completed induction with ABA + MTX. In moderately to severely active RA and JIA patients, a relationship between ABA Cmin and efficacy was observed. Therefore, this analysis in very early RA patients, reports on the pharmacokinetics (PK) and immunogenicity of ABA and the maintenance of remission during the DE period of AVERT-2.

Objectives: To assess the relationship between changes in ABA exposure and the maintenance of remission and the effect of immunogenicity on exposure during the DE period of AVERT-2.

Methods: Pts received blinded SC ABA (125mg once wky [QW]) + MTX or ABA PBO + MTX induction treatment for 56 wks. Pts who completed induction with ABA + MTX and had sustained SDAI remission (≤3.3 at Wks 40 and 52) were re-randomized 1:1:1 to ABA QW + MTX for 48 wks (Arm C), ABA every other wk (EOW) + MTX for 24 wks followed by ABA PBO + MTX for 24 wks (Arm D), or ABA QW + MTX PBO for 48 wks (Arm E) in the DE period. ABA trough (Cmin) and anti-drug antibody (ADA) samples were collected in all subjects during the DE period. Serum ABA concentrations and ADA were measured using a validated enzyme immunoassay method and an electrochemiluminescence assay, respectively. Efficacy endpoints included change from DE Day 1 in SDAI score, HAQ-DI score, Physician's Global Assessment (PhGA), and tender (TJC) and swollen (SJC) joint counts. The relationship between ABA Cmin and efficacy endpoints were assessed. Additionally, the impact of immunogenicity on ABA Cmin was explored.

Results: Mean ABA Cmin values remained stable throughout the DE period for subjects in Arms C and E. ABA Cmin values decreased by ~50% in subjects in Arm D for the first 24 weeks from the start of DE and were ~0 for weeks 24-48 consistent with the change in the frequency of ABA dosing from EOW to ABA withdrawal (Figure 1 top).

The incidence of immunogenicity appeared to increase upon withdrawal of ABA in Arm D. ADA formation did not appear to affect ABA Cmin, as ABA Cmin remained consistent between pts with and without ADA.

Upon withdrawal of ABA in Arm D, there appeared to be an increase in the mean change from baseline (Day 1 of DE) in SDAI over time, which followed a similar time course as the washout of ABA (Figure 1 bottom). Similar results were observed for other efficacy endpoints such as HAQ-DI, PhGA, TJC, and SJC.

Conclusion: The PK data in these early onset, MTX-naive, ACPA+ RA pts correlated well with the maintenance of remission in Arms A and E. Tapering of ABA from EOW to MTX only in Arm D results in a corresponding decrease in ABA Cmin, an increase in positive antibody response, and loss of remission.

References:

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