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Risk factors for developing diseases or comorbidities

OP0073 PERFORMANCE OF THE EULAR DEFINITION OF ARTHRALGIA SUSPICIOUS FOR PROGRESSION TO RHEUMATOID ARTHRITIS – A LONGITUDINAL STUDY

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Background: Recently a European League Against Rheumatology (EULAR)-taskforce has defined arthralgia suspicious for progression to rheumatoid arthritis (RA)¹, in order to allow inclusion of homogeneous sets of arthralgia patients in clinical studies. This was done as the field is currently shifting towards performing trials in very early disease phases as there is growing evidence that very early treatment initiation allows better disease modification and treatment of arthralgia may even prevent the development of RA. The definition was developed with the clinical expertise as reference. It is intended for use in arthralgia patient that rheumatologists consider to be at risk for progression to RA.

Objectives: To longitudinally evaluate the EULAR definition of arthralgia suspicious for progression to RA in: (1) patients in whom rheumatologists felt that imminent RA was more likely than other arthralgia's (Clinically Suspect Arthralgia, CSA); this target population fulfils the entry criterion and (2) in arthralgia patients referred to secondary care prior to rheumatologic evaluation; in these patients the entry criterion was ignored.

Methods: The definition was assessed in 241 Dutch CSA-patients and 113 patients referred to the Umeå university hospital with recent-onset arthralgia in small joints. The external reference was arthritis development <2-years follow-up.

Results: CSA-patients with a positive definition ($\geq 3/7$ parameters present) had an increased risk on arthritis development compared to definition-negative CSA-patients (HR 2.1, 95% CI 0.9–4.7). The sensitivity of a positive definition was 84% and the positive predictive value (PPV) 30%. In arthralgia patients in whom the definition was applied prior to rheumatologic evaluation, a positive definition was neither sensitive (10%) nor predictive (PPV 3%). Sensitivity analyses with fulfilment of the 2010 criteria for RA or initiation of DMARDs <2-years of follow-up as external reference showed similar results.

Conclusions: The EULAR definition of arthralgia suspicious for progression to RA is sensitive when used to support the expert's opinion on imminent RA. It was not discriminative in patients without prior rheumatologic evaluation. These data suggest that the definition should be used as designed and serves to further homogenize patients that rheumatologists consider at risk for RA.

References:

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OP0074 ASSOCIATION BETWEEN A HISTORY OF MYCOBACTERIAL INFECTION AND THE RISK OF SJÖGREN'S SYNDROME: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

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Background: An increased risk of tuberculosis (TB) has been found in subjects with Sjögren's syndrome (SS); however, whether TB or nontuberculous mycobacteria (NTM) infection is associated with the risk of SS is still unknown.

Objectives: To explore the association between a history of mycobacterial infection and the risk of newly diagnosed SS.

Methods: After excluding those who had rheumatoid arthritis and systemic lupus erythematosus, we identified 5,751 newly diagnosed SS cases and 86,265 non-SS patients matched (1:15) for age, sex, and the year of first diagnosis date as controls using nationwide, population-based, claims data. The association between the risk of incident SS and a history of treated mycobacterial infection, including TB and NTM, was quantified by odds ratios (ORs) with 95% confidence intervals (CIs) using conditional logistic regression analysis after adjusting for Charlson comorbidity index (CCI) and bronchiectasis.

Results: The mean \pm SD age was 55 ± 14 years and the proportion of female gender was 87.8% in newly diagnosed SS cases and non-SS controls. An association was observed between NTM infection (OR, 11.24; 95% CI, 2.37–53.24) and incident SS, but not between TB infection and incident SS (OR, 1.29; 95% CI, 0.97–1.71) after adjustment for CCI and bronchiectasis. The magnitude

of the association between NTM and SS risk was greatest among those aged between 45 and 65 years (OR, 39.24; 95% CI, 3.97–387.75).

	Univariable analysis OR (95% CI)	Multivariable analysis OR (95% CI)
Nontuberculous mycobacteria	20.00 (4.48–89.36)	11.24 (2.37–53.24)
Tuberculosis	1.86 (1.41–2.45)	1.29 (0.97–1.71)
CCI ≥ 1	1.89 (1.77–2.01)	1.83 (1.71–1.94)
Bronchiectasis	3.19 (2.76–3.69)	2.74 (2.36–3.18)

Conclusions: The present study demonstrates a statistically significant association of newly-diagnosed SS with a history of NTM, but not TB infection.

References:

- [1] Peri Y, Agmon-Levin N, Theodor E, et al. Sjogren's syndrome, the old and the new. *Best practice & research Clinical rheumatology* 2012;26(1):105–17.
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OP0075 OSTEOPOROTIC FRACTURE RISK ASSESSMENT USING FRAX FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Bone loss and fractures following hematopoietic stem cell transplantation (HSCT) is common,^(1, 2) and identifying patients at high risk for osteoporotic fractures following HSCT remains challenging. In the general population, the World Health Organization fracture risk assessment tool - FRAX is utilized to estimate a patient's 10-year probability of developing a major osteoporotic fracture and hip fracture.⁽³⁾ However, the utility of the FRAX model in predicting fractures following HSCT has not been evaluated.

Objectives: To assess the predictive value of FRAX in osteoporotic fracture risk assessment following HSCT.

Methods: We conducted a retrospective cohort study of patients >18 years that received a HSCT at The University of Texas MD Anderson Cancer Center, from January 1, 2001 to December 31, 2010. Patients were considered to have entered the cohort at the time of HSCT. All patients were retrospectively followed until December 31, 2013 for assessment of osteoporotic fracture. Osteoporotic fractures following HSCT were identified using ICD-9 codes, and confirmed by radiology and physician documentation. FRAX probabilities were calculated from baseline information obtained by chart review.

Results: A total of 5,170 patients underwent a HSCT during the 10-year study period. During an average of 3.3 years of follow up, 10% of patients developed a fracture. Fracture rates were higher (14%) in patients that underwent an autologous HSCT in comparison to those that received an allogeneic HSCT (6%). Mean major osteoporotic fracture FRAX scores were significantly higher in individuals who sustained an osteoporotic fracture compared to individuals who did not. The area under the receiver operating characteristic curve at 5 and 10 years following the HSCT were 0.61 and 0.66 respectively (Figure). We assessed the ability of the FRAX model for prediction of osteoporotic fracture with and without considering death as a competing risk. The hazard ratios were similar for both models (HR, 2.63, 95% CI, 1.93, 3.59; HR, 2.54, 95% CI, 1.86, 3.47, respectively).

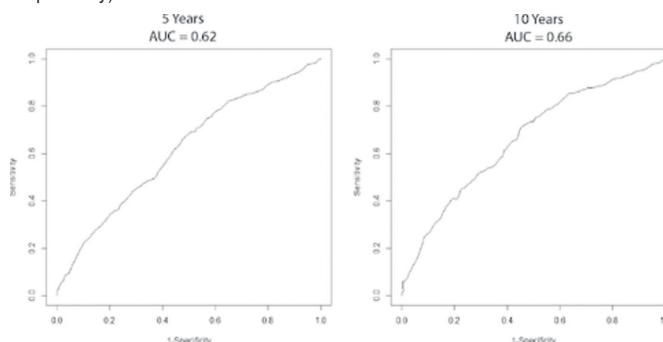


Figure 1

Conclusions: To the best of our knowledge, this is the first study to demonstrate that the FRAX model has modest discriminative ability in predicting osteoporotic fractures following HSCT. Further independent validation of our findings is necessary, before routinely using the FRAX model in clinical practice.

References:

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OP0076 RISK OF DEVELOPING ADDITIONAL IMMUNE MEDIATED MANIFESTATIONS FOR PATIENTS WITH SYSTEMIC ARTHRITIDES

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Background: Patients with the systemic arthritides ankylosing spondylitis [AS], psoriatic arthritis [PsA], rheumatoid arthritis [RA] may develop additional, non-musculoskeletal immune mediated manifestations (nms-IMMs).

Objectives: To compare the risk of developing nms-IMMs between patients with and without an existing AS, PsA, or RA.

Methods: Risk for nms-IMMs was estimated in the MarketScan Commercial Claims and Encounters database (1/2006–9/2015) for case patients with AS, PsA, RA (the “systemic arthritides”). Up to 1,000 controls were matched with replacement by age, sex, state of residence and insurance type to case patients aged 18–64. The systemic arthritides (“cases”) were identified by ICD-9 diagnosis codes on ≥2 medical claims ≥30 days apart. A case patient’s earliest nms-IMM claim was designated as the index date for the case and all matched controls. Onset of 6 nms-IMMs was identified by the first post-index claim: celiac disease [CE], hidradenitis suppurativa [HS], inflammatory bowel disease [IBD], lupus [SLE], psoriasis [PsO], uveitis [UV]; some of these are well-known manifestations of seronegative spondylarthropathies, like PsA and AS; some are not. All subjects had continuous health plan enrollment for ≥365 days before and after index date. Cumulative incidence of nms-IMMs was assessed at 5 years. Their risk was analyzed with stratified Cox proportional hazards models. Standard errors were adjusted for clustering by case-control match group.

Results: Among 117,794 cases, mean age was 49 years and 71% were female. Mean number of matched controls per case was 664. Across the 3 initial cohorts of patients with AS, PsA, or RA, median follow-up ranged 939–972 days for cases and 931–950 days for controls. Among case patients, 5-year cumulative incidence of any nms-IMM occurrence was 17.5% for AS, 41.8% for PsA, and 14.4% for RA. Patients with nms-IMMs had significantly higher risk than matched controls of developing each, any 1, or any 2 of the 6 manifestations ($P \leq 0.002$) (Table).

Initial IMID	Secondary IMID							
	CE	HS	SLE	PsO	UV	IBD	1 st of Any 1	2 nd of Any 2
AS	N Cases	6,339	6,344	6,282	6,275	6,103	6,352	6,352
	5-yr Incidence	0.9	0.2	2.9	4.2	7.7	3.4	17.5
	Hazard Ratio	11.2	3.3	23.7	8.6	54.9	16.0	24.6
PsA	N Cases	8,382	8,389	8,311	6,111	8,351	8,347	8,406
	5-yr Incidence	0.5	0.6	2.1	51.0	1.8	1.7	41.8
	Hazard Ratio	5.3	10.5	14.1	163.2	10.0	7.3	50.9
RA	N Cases	102,708	102,810	100,414	101,965	102,424	102,318	103,036
	5-yr Incidence	1.0	0.5	7.5	3.4	1.5	1.8	14.4
	Hazard Ratio	10.3	8.1	55.3	7.2	8.2	7.6	14.1

Notes: Hazard ratios from Cox proportional hazards models. Hazard ratios >1 indicate higher risk for case patients relative to controls. All hazard ratios are significant at $P < 0.002$.

Conclusions: The risk of developing non-musculoskeletal manifestations was significantly higher for patients with AS, PsA, and RA than for matched controls. These included not only the well-known manifestations of PsA and AS but also others like manifestations leading to claims for SLE, celiac disease or HS. When managing these systemic arthritides, surveillance for additional immune mediated manifestation is warranted.

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OP0077 PRIMARY PROPHYLAXIS FOR PNEUMOCYSTIS PNEUMONIA IN PATIENTS WITH RHEUMATIC DISEASE AND TREATED WITH PROLONGED, HIGH-DOSE STEROID: A RETROSPECTIVE COHORT STUDY WITH 12-YEAR OBSERVATION

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Background: Pneumocystis pneumonia (PCP) is a significant cause of morbidity and mortality in patients with rheumatic diseases, especially in the case of patients receiving high-dose steroid treatment.

Objectives: To investigate the efficacy and safety of PCP prophylaxis using trimethoprim/sulfamethoxazole (TMP-SMX) in patients with rheumatic disease receiving prolonged, high-dose steroids

Methods: This study includes 1522 cases of prolonged (≥4 weeks), high-dose (≥30mg/day prednisone or equivalent) steroid treatment from 1092 patients with any rheumatic diseases during a 12-year period in a single tertiary referral center in South Korea. Of them, prophylactic TMP-SMX was administered in 262 cases (prophylaxis group) with a mean (SD) duration of 229.0 (272.7) days whereas other 1260 cases received no prophylaxis (control group). Primary outcome was 1-year incidence of PCP between the two groups. Secondary outcomes included PCP-related mortality, ICU admission rate, all-cause in-hospital mortality and incidence of any adverse drug reactions (ADRs) of TMP-SMX. To minimize the baseline imbalance between the two groups, we introduced propensity-score matching and performed the same analysis in the post-matched population as a sensitivity analysis.

Results: Patients in the prophylaxis group were treated more often with secondary immunosuppressive drugs and had a higher proportion of patients with PCP high-risk diseases (ANCA-associated vasculitis and dermatomyositis) and lymphopenia at baseline. Overall, 30 cases of PCP occurred and resulted in death in 11 cases (36.7%). In the prophylaxis group, only one non-fatal case of PCP occurred. One-year PCP incidence was significantly lower in the prophylaxis group (adjusted HRs=0.096 [0.013–0.719]) (Figure). TMP-SMX also significantly reduced the PCP-related mortality (adjusted HR=0.101 [0.001–0.809]) whereas

PCP free survival

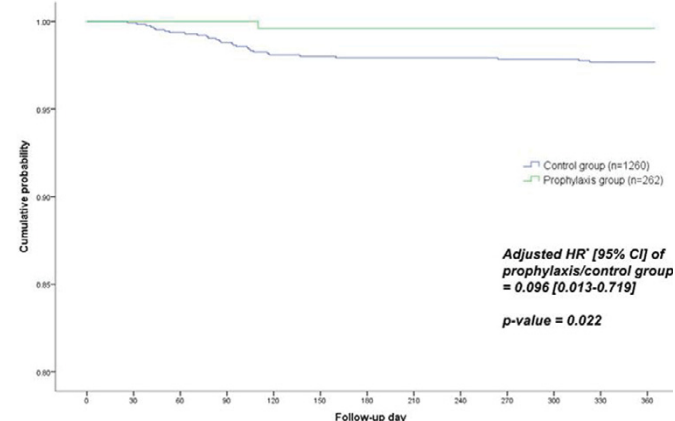


Figure. Kaplan-Meier curve of 1-year incidence of PCP between the two groups

*. HR was adjusted for patient's age, concomitant cyclophosphamide pulse and baseline lymphopenia