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14-3-3eta Synergistically Interacts with Anti-CCP2 Status and Simple Disease Activity Index (SDAI) Levels to Predict Rapid Radiographic Progression over the Following Year in Patients with Inflammatory Polyarthritis

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Objectives: Our objective is to examine whether HIGH 14-3-3 η levels add significantly to anti-CCP2 positivity and elevated Simple Disease Activity Index (SDAI) levels measured at the same visit to predict rapid radiographic progression (RRP) over the following year. We previously reported that baseline 14-3-3 η levels ≥ 0.50 ng/ml (HIGH 14-3-3 η) were predictive of radiographic progression over 5 years, as were the serial 14-3-3 η changes in serum levels over the course of disease.

Methods: The Sharp/van der Heijde (SvH) and SDAI scores, serum 14-3-3 η and anti-CCP2 were all measured at initial and yearly follow up visits in patients with recent onset polyarthritis treated to remission. HIGH 14-3-3 η was defined as ≥ 0.50 ng/ml; anti-CCP2 positivity as ≥ 5 U/ml (EuroImmuno); elevated SDAI as > 11 ; RRP as an increase of ≥ 5 Units in the Erosion component of the SvH score. Generalized Estimated Equations (GEE) were performed to assess the association with RRP of elevated SDAI, positive anti-CCP2 and HIGH 14-3-3 η , alone and in combination.

Results: Mean age was 58.5 years, 61.2% female; median duration at inclusion 3.4 months; median (IQR) follow-up 17.6 (9.0-33.5) months. Out of 1529 complete evaluations in 533 patients, 511 (33.4%) were HIGH 14-3-3 η , 590 (38.6%) anti-CCP2 positive and 722 (47.2%) elevated SDAI. In univariate analyses, HIGH 14-3-3 η , anti-CCP2, and elevated SDAI were each associated with significantly increased Relative Risks (RR) of RRP: 1.82 (1.36-2.43) $p < 0.0001$; 2.33 (1.65-3.30) $p < 0.0001$; and 1.80 (1.38-2.34) $p < 0.0001$, respectively. In GEE, relative to being negative for all three, being positive for all of HIGH 14-3-3 η , anti-CCP2, and elevated SDAI was associated with an increased RR of 4.67 (2.77-7.86), RRP then occurred following 25.5% of such visits. Being positive for only 2 variables identified subsets of patients at intermediate RR (2.61 to 4.42) depending on the combination, while only 1 positive variable was associated with lower RR (0.93 – 1.98) depending on the variable. The contribution of 14-3-3 η was highest in patients with either anti-CCP2 positive or elevated SDAI alone.

Conclusion: In this cohort of patients with polyarthritis treated to remission, the presence of HIGH 14-3-3 η amplified the risk for RRP conferred by anti-CCP2 and/or active disease. The highest risk of RRP over the following year was present in anti-CCP2 positive patients who also had active disease and HIGH 14-3-3 η levels. Adding 14-3-3 η measurement to anti-CCP2 and clinical measures over the course of RA may inform therapeutic strategies tailored to halt rapid joint damage progression in the most susceptible patients.

2

Suboptimal Immunization Coverage Among Rheumatology Patients in Routine Clinical Care

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Objectives: Vaccine-preventable infections pose an increased risk of disease and complications in patients with systemic autoimmune rheumatic diseases (SARD). As such, while recommendations highlight the importance of vaccination in this at-risk population, immunization coverage remains largely unknown. We assessed vaccination rates and predictors of vaccination among rheumatology patients in routine clinical care.

Methods: Consecutive patients presenting to a tertiary rheumatology clinic at the McGill University Health Center between May and September 2015 were asked to fill a survey on vaccination. Patients self-identified as having rheumatoid arthritis (RA) (RA, juvenile idiopathic arthritis), SARD (e.g., vasculitis, lupus, systemic sclerosis, myositis), spondyloarthropathies (SpA) (psoriatic arthritis, ankylosing spondylitis), or other diseases (Other). Multivariate logistical regression analyses were performed to evaluate patient and physician factors associated with vaccination rates (influenza, pneumococcus, hepatitis B virus [HBV], and herpes zoster [HZ]).

Results: 352 subjects were included in the analysis (RA:135, SARD:113, SpA:48, Other:56). Vaccination rates were reported as: (1) influenza: RA 48.1%, SARD 42.0%, SpA 33.3%, Other 48.1%; (2) pneumococcus: RA 41.5%, SARD 37.8%, SpA 31.6%, Other 16.3%; (3) HBV: RA 34.0%, SARD 55.6%, SpA 71.4%, Other 36.8%; and (4) HZ: RA 3.2%, SARD 9.5%, SpA 17.6%, Other 7.0%. In multivariate analyses, physician recommendation was the strongest independent predictor of vaccination across all vaccine types (influenza: odds ratio (OR) 12.6, 95% confidence interval (CI) 5.40-29.6; pneumococcus: OR 424, 95% CI 99.7-1801; HBV: OR 12.8, 95% CI 5.27-31.1). Patient-reported awareness of the benefits of vaccination was also a significant predictor of vaccination (influenza: OR 5.15, 95% CI 1.26-21.1; HBV: OR 11.5, 95% CI 2.49-52.8). The effect of age varied by vaccine (influenza: OR 1.04, 95% CI 1.02-1.06; HBV: OR 0.96, 95% CI 0.94-0.99). There were no other significant associations with vaccination, including disease group, disease duration, comorbidities (cancer, diabetes, renal disease), treatment type (disease-modifying anti-rheumatic drugs and/or biologics), and access to a primary care physician.

Conclusion: Despite national guidelines and recommendations for vaccination in this at-risk population, immunization coverage against influenza, pneumococcus, HBV, and HZ is far from optimal among ambulatory rheumatology patients. An important role for both patient and physician education is highlighted from our study as both patient awareness of the benefits of vaccination, and physician recommendation were strongly predictive of vaccine uptake. These results will help inform strategies aimed at optimizing vaccination rates in this at-risk population. Best Abstract by a Medical Student

3

Citrullinated Provisional Matrix Proteins Influence Fibroblast Activation

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Objectives: Considering that both citrullination and activated fibroblasts are hallmarks of

several chronic inflammatory conditions, including malignant cancers, lung fibrosis, and rheumatoid arthritis (RA)—and that especially in the case of RA, these are both correlated with a severe disease course—our objective is to better understand how citrullinated provisional matrix proteins may influence the initiation and maintenance of activated fibroblast phenotypes.

Methods: Fibronectin, the primary adhesive matrix protein for fibroblasts within inflammatory environments, was citrullinated using a mixture of PAD2 and PAD4 enzymes. Cell phenotypes, primarily including adhesion, spreading, migration, and mechanosensing capacity, were evaluated through a combination of fluorescence microscopy, time-lapse microscopy, and atomic force microscopy (AFM), respectively. To begin elucidating the mechanism underlying observed phenotypic differences, mass spectroscopy (MS) was performed on citrullinated fibronectin (Cit-Fn) to identify specific regions of modification, and a Systematic Analysis of PTM Hotspots (SAPH-ire) was performed to evaluate which of these regions possesses the most probable biological significance. We explored the impact of these modifications on specific integrin subtypes by studying the ability of CHO cells transfected with single integrin subtypes to interact with Cit-Fn. Integrin preference and focal adhesion formation, along with associated downstream signaling, were analyzed using a combination of confocal microscopy and magnetic bead force-inducible co-immunoprecipitation assays.

Results: Phenotypic assays determined that healthy fibroblasts possess a decreased ability to attach and spread on Cit-Fn. Despite this deficit in attachment, however, AFM results show that fibroblasts on Cit-Fn are on average stiffer, indicating that mechanotransduction pathways are activated which allow the cells to interpret their environments as being stiff and to react in kind. One such resulting reaction is an enhanced migratory capacity as determined by improved defect closure in wound healing assays. Underlying these altered phenotypes are at least 20 unique sites of fibronectin citrullination, as identified by MS, three of which reside in the integrin binding domain and are predicted by SAPH-ire to have the largest biological impact. CHO adhesion assays, in part, confirm this prediction demonstrating that $\alpha v \beta 3$ integrin binding on Cit-Fn is detrimentally impacted. In consequence, $\alpha 5 \beta 1$ integrins appear to compensate by both increasing in abundance and recruiting additional integrin subunits and downstream signaling molecules, notably phospho-FAK and vinculin.

Conclusion: By itself, citrullination of fibronectin fundamentally alters how fibroblasts interact with the matrix, ultimately resulting in enhanced migratory capacity. An integrin switch, whereby $\alpha 5 \beta 1$ dominates over $\alpha v \beta 3$ in fibroblast attachment and subsequently enacts mechanotransduction signaling pathways, underlies this altered behavior. Best Abstract by a Post-Graduate Research Trainee

4

Evaluating the Effectiveness of a Faculty-Resident Co-Learning Quality Improvement Curriculum

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Objectives: One of the greatest challenges in quality improvement (QI) training is the lack of faculty experts who can teach and supervise QI projects. We implemented a faculty-resident co-learning QI curriculum, where faculty and residents experienced the curriculum together, which we hypothesized would allow faculty to role model the importance of QI. The purpose of our study was to evaluate the impact of the co-learning approach on resident knowledge of QI.

Methods: From July 2013 through June 2017, the authors conducted a yearly co-learning QI

curriculum for the Division of Rheumatology at the University of Toronto. Faculty and resident participants learned together using didactic and interactive formats. Project work occurred between sessions, and at the end of the year, all programs presented their projects at a multidivisional QI half-day. We compared our model to 4 other Ontario rheumatology programs where a range of QI educational experiences exist (didactic rounds, reading materials, case based discussions, interactive role plays, and discussion of QI projects). We evaluated our program by collecting descriptive data from workshop evaluations. We conducted a year-end objective structured clinical exam (OSCE) in 2016 and 2017, where all Ontario rheumatology residents were presented a QI problem and had to identify an aim, a set of measures and potential QI interventions. They were evaluated using the Quality Improvement Knowledge Assessment Tool (QIKAT), a validated tool of QI assessment. The results of the OSCE station was examined using a non-parametric Wilcoxon rank sum test.

Results: Twenty-eight rheumatology residents had gone through the co-learning curriculum. Ninety-two percent (49 of 53 workshop evaluations) felt the course was excellent or outstanding and the majority felt it improved their QI knowledge and skills. Nineteen University of Toronto rheumatology residents and 29 other rheumatology residents completed the QI OSCE station. Residents who completed the co-learning QI curriculum scored higher on the QI station than other residents (Median 8/10 vs. 7/10, $p=0.0015$). PGY5 residents who completed the co-learning project scored higher than PGY4 residents at U of Toronto who did not complete the project (Median 9/10 vs. 7/10, $p=0.0024$), and higher compared to other residents (Median 9/10 vs. 7/10, $p<0.0001$).

Conclusion: We improved resident learning by better preparing faculty to do and teach QI using the co-learning framework. This was a small sample size and will be the basis for future work. Collaboration amongst schools to share QI resources and expertise may help improve QI skills for all rheumatology trainees.

5

Impact of Maternal Systemic Autoimmune Rheumatic Diseases (SARDs) on Neonatal Outcomes: A Population-Level Analysis

Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Anamaria Savu (University of Alberta, Edmonton); Padmaja Kaul (University of Alberta, Edmonton)

Objectives: We examined the association between SARDs and neonatal outcomes in a contemporary pregnancy cohort in the province of Alberta, Canada

Methods: The patient population consisted of women giving birth between January 1, 2005 to December 31, 2014 ($n=312,081$). For women with multiple gestations during the period, one birth event was randomly selected. Women with SARDs included any of the following: systemic lupus erythematosus (SLE), systemic sclerosis, myositis and sjogren's syndrome, diagnoses based on the presence of International Classification of Disease version 9/10 codes in outpatient or inpatient records. Baseline characteristics, comorbidities, medication use (available for all births after January 1, 2009), and neonatal outcomes among women with and without SARDs were compared.

Results: Compared to women with no SARDs ($n=311,755$), women with SARDs ($n=326$, 0.1%) were slightly older (SARDs 31.3 vs No SARDs 29.3 years ($p<0.01$)) but did not differ in terms of rural residence, ethnicity, median household income or nulliparity. Of the 326 women with SARDs, 271 (83.1%) had SLE, 53 (16.3%) had systemic sclerosis, 26 (8%) had dermatomyositis, 17 (5.2%) had polymyositis and 29 (8.9%) had sjogren's syndrome. Rates of pre-term delivery, emergent caesarean section, induction, hypertensive disorders/eclampsia and

mortality were higher among women with SARDs than those with no SARDs. Offspring of women with SARDs had lower birth weights, were more likely to have small for gestational age babies (SGA), and had longer stays in neonatal ICU. Among women with SARDs, prescription rates in the 270 days prior to delivery were highest for anti-malarials (25.1%) followed by steroids (16.3%). Regarding the impact of medication use during pregnancy, the unadjusted odds ratio was significant for steroids on preterm delivery (OR 3.84 (95% CI 1.66, 8.89, $p < 0.05$) and hypertensive disorders of pregnancy (OR 3.67 (95% CI 1.51, 8.93), $p < 0.05$); for nonsteroidal anti-inflammatories, the unadjusted odds ratio was significant for preterm delivery (OR 4.96 (95% CI 1.55, 15.85, $p < 0.05$). Antimalarials did not have an impact on pregnancy related outcomes in the unadjusted analysis. After multivariable adjustment, both NSAID use (OR (95% CI): 5.24 (1.57, 17.52), $p < 0.01$) and steroid use (OR (95% CI): 3.15 (1.31, 7.59), $p < 0.01$) were significantly associated with a higher risk of preterm delivery.

Conclusion: Women with SARDs are at an increased risk of adverse outcomes during pregnancy. The association between corticosteroid and NSAID use and preterm delivery requires further investigation. Our findings suggest the need for closer monitoring and coordinated care with obstetrics and perinatology in these high risk women.

6

Effectiveness of the Outreach Model for Rheumatology Specialty Clinics to On-Reserve First Nations in Alberta: System-level and Individual Measures of Performance and Outcomes

Sujay Nagaraj (University of Calgary, Calgary); Claire Barber (University of Calgary, Calgary); Margaret Kargard (Siksika Health Services, Siksika); Tyler White (Siksika Health Services, Siksika); Cheryl Barnabe (University of Calgary, Calgary)

Objectives: A model of care consisting of rheumatology specialty services embedded in the primary care context was instituted to reduce barriers to care and improve treatment outcomes for First Nations persons with Inflammatory Arthritis (IA) in one community. We assessed the system-level performance of the model as well as its effectiveness on disease activity measures and patient-reported outcomes over 7 years.

Methods: Patients were enrolled in a longitudinal cohort at the Siksika Nation in Alberta (2011-2017). Clinical characteristics, disease activity measures, and treatment recommendations were systematically recorded over follow-up. System-level performance was evaluated according to established measures developed by the Arthritis Alliance of Canada. Mixed-model regression analysis was performed to determine monthly rates of change for disease activity measures, adjusted for baseline demographics and disease activity measures.

Results: 59 participants (78% female, mean age 47 (SD 13)), predominantly with RA ($n=36$), were followed for a mean of 29 (SD 23) months with a mean of 6 (SD 5) visits per participant. At the system-level, the 50th and 90th percentile wait times were 69 and 695 days, respectively. Only 33% of patients were seen in the benchmark waiting time of 4 weeks but 83% of patients were followed up in each measurement year. Nearly all (96%) of patients received a DMARD in each measurement year and 90% were prescribed a DMARD within 2 weeks of diagnosis. At the baseline visit, 72% of participants with RA were in DAS28 moderate or high disease activity state. Disease-modifying agents were escalated for moderate or high disease activity at 65% of visits for RA with reasons for not escalating including pending investigations, being too soon to assess response to a new therapy, patient choice, contraindication to therapy, absence of joint swelling, or intra-articular injections provided. Swollen and tender joint counts significantly improved during follow-up (SJC28 -0.20, 95%CI -0.29 to -0.10; TJC28 -0.20, 95%CI -0.34 to -

0.01, both $p < 0.001$). Pain (0.01, 95% CI -0.05 to 0.05, $p = 0.97$), physician global evaluation score (-0.05, 95% CI -0.11 to 0.06, $p = 0.08$), and HAQ (-0.01, 95% CI -0.01 to 0.01, $p = 0.45$) did not significantly improve over time. Patient global evaluation score continued to worsen over time (0.08, 95% CI 0.03 to 0.13, $p = 0.002$).

Conclusion: The program met several system-level performance measure targets however patients still experienced long wait times. Despite improvement in swollen and tender joint counts and adherence to current treatment paradigms, patient-reported outcomes did not significantly improve during follow-up. Further innovation is required to meet relevant outcomes. Best Abstract by an Undergraduate Student

7

Preventing Rheumatoid Arthritis (Pre-RA): Preferences of Potential Recipients, Patients, and Health Care Professionals for Preventative Treatment

Mark Harrison (University of British Columbia/Arthritis Research Canada, Vancouver); Nick Bansback (University of British Columbia/Arthritis Research Canada, Vancouver); Luke Spooner (University of British Columbia, Vancouver); Cheryl Koehn (Arthritis Consumer Expert, Vancouver); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal)

Objectives: To (1) determine preferences of patients with rheumatoid arthritis, first-degree relatives (FDRs) of patients (as a proxy for pre-symptomatic, at risk people), and health care professionals (HCPs) for preventative treatment, and (2) predict the likely uptake of preventative treatments.

Methods: A discrete choice experiment with 5 key attributes of treatment (reduction in risk of RA, how treatment is taken, chance of side effects, certainty in estimates, their HCPs/patients opinion) was administered using a web survey to Canadian patients and FDRs of patients, and HCPs. This survey asked participants to first choose between sets of 2 hypothetical preventative RA treatments, then choose between their preferred treatment and 'no treatment for now'. DCE data was analyzed using conditional logit regression model to estimate the significance and relative importance of attributes in influencing preferences and a mixed logit model to explore preference heterogeneity.

Results: 78 patients, 30 FDRs and 47 HCPs from nine Canadian provinces started and completed all tasks in the survey. HCPs were primarily rheumatologists (81%) or rheumatology nurses (9%). Patients (86%) and FDRs (73%) were predominantly female; patients were older (6% aged 18-39) than FDRs (23% aged 18-39). Preferences for levels within attributes were in the expected direction. The preference of the patient was the most influential attribute for HCPs (patient prefers vs. does not prefer: $\beta 0.734$, $p < 0.001$), followed by reduction in the risk of developing RA (risk reduced from 60 in 100 to 24 in 100 vs. 44 in 100) $\beta 0.509$, $p < 0.001$). The opinion of HCPs was also important to patients and FDRs (patients: $\beta 0.461$; FDRs: $\beta 0.379$), along with risk reduction (patients: $\beta 0.413$; FDRs: $\beta 0.430$). FDRs had stronger preferences for how treatment was taken (oral vs infusion: $\beta 0.355$, $p = 0.010$) than patients ($\beta 0.257$, $p = 0.010$) or HCPs ($\beta 0.257$, $p = 0.010$). Predicted uptake suggested that 19% of FDRs would not be willing to take any currently available treatment as preventative treatment, while 4% of HCPs wouldn't be willing to recommend a preventative treatment. HCPs were predicted to prefer non-biologic DMARDs (e.g. oral methotrexate 35%; hydroxychloroquine 19%) than biologic DMARDs (e.g. abatacept 5%); FDRs preferred non-biologic DMARDs (oral methotrexate 24%; hydroxychloroquine 32%) and other options like statins (65%).

Conclusion: Uptake of preventative strategies will be most influenced by discussions of

preferred options between providers and recipients, potential risks and benefits, and convenience. This evidence will help policy makers identify the most likely preventative treatment strategies to be acceptable to at-risk people. Supported by a CIORA grant

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A Pragmatic Pilot Randomized Controlled Trial of the OA Go Away, a Symptom and Exercise Tracking Self-Management Behavioural Intervention for Promoting Adherence to Physical Activity Among Individuals with OA of the Hip or Knee

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Objectives: Despite the well-established benefits of exercise and physical activity, the majority of Canadians with OA of the hip or knee do not meet Health Canada guidelines for physical activity. Behavioural interventions are needed to help patients make the transition from supervised structured health care provider care to long term independent self-management. The objectives of this study were to assess the feasibility of conducting a full RCT to test the effectiveness of the OA Go Away self-management behavioural intervention and to determine its acceptability. The OA Go Away is an internal reinforcement adherence measure that includes a monthly personalized self-report symptom tracker, goals and action plan and a weekly exercise log.

Methods: This study was a 3-month pragmatic pilot-test of the OA Go Away. 40 participants with OA of the hip or knee were randomized into either the treatment group who used the OA Go Away for 3 months, or the control group who received standard care at The Arthritis Society. Participants completed outcome measures at baseline and at 3 months. Outcomes were compared between study groups at the end of the trial using Mann-Whitney and 2-tailed Fisher's exact tests to assess adherence to prescribed exercise, level of physical activity, functional goal attainment, pain, stiffness, physical function, and quality of life. Treatment group participants completed a measure to determine the usefulness and acceptability of the OA Go Away.

Results: 36 participants (16 in the treatment group and 20 in the control group) completed the protocol. At the end of the trial, participants in the treatment group were more physically active ($p=0.02$), had less pain ($p=0.03$), better function ($p=0.048$) and more vitality ($p=0.01$). Adherence, goal attainment and other quality of life scores, were greater in the treatment group but were not statistically significant. The majority of participants in the treatment group felt that the OA Go Away was acceptable in terms of time commitment, useful and motivational. Some of the participants proposed that an electronic version of the OA Go Away would facilitate visualization of changes in status, exercise progress and achievement of goals.

Conclusion: This pilot RCT justifies a formal randomized controlled trial of the OA Go Away and shows promising results concerning its acceptability and effectiveness. Its real potential may be best realized if translated into an electronic tool.

9

Disparities between Ultrasound and MRI Assessment of Erosions: Are they Dependent on Size and Location?

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Objectives: Compared to Magnetic Resonance Imaging (MRI), studies have reported a high

specificity of ultrasound (US) detection of bone erosions joints in patients with RA, but only low/moderate sensitivity. However, the nature of the US probe does not allow for erosions to be seen in regions directly adjacent to other bones. When examining sensitivity and specificity, this is an important factor to consider. Thus, we evaluated US assessment of erosions in the metatarsophalangeal joints (MTPJ) by characterizing the location of erosions on MTPJ bones observed by MRI.

Methods: Patients newly diagnosed with RA (ACR criteria) were recruited. Using US, the presence of erosions on 2nd-5th MTPJ was recorded. The same foot was imaged using MRI. Metatarsal heads and phalangeal bases were sectioned into dorsal, plantar, medial and lateral regions. Blinded to US results, a radiologist recorded the locations and grades (OMERACT criteria, grades 0-10) of MRI erosions on each bone of the 2nd-5th MTPJ. Dorsal and plantar surfaces and lateral 5th MTPJ were hypothesized to be within the field-of-view of US. We described the location and size of erosions seen on MRI, and compared these with erosions seen on US.

Results: This study included 39 patients [n=33 female, mean (SD) age=51.6 (10.3) years]. MRI found erosion grade ≥ 1 in 123 MTPJ bones (26 on the phalanx base, 97 on MTP head), totaling 101 unique joints (of 156 total) affected by erosion. The majority of erosions were grade 1 [n=107 (87%)]. Erosions were most common on the plantar surface [n=110 (89.4%)], with few on dorsal, medial or lateral surfaces of the bones (n=5, 21 and 38 respectively). Despite MRI identifying 90 joints with erosions in regions hypothesized to be within the US field-of-view (57.7% of 156 joints), these erosions were rarely visualized on US (n=5). Of 14 MTPJ with MRI erosion grade ≥ 2 in either bone, US visualized erosions in 4 joints. US found erosion in 2 joints that were not seen on MRI.

Conclusion: Most MRI erosions in the MTPJs were on the plantar surface which can hypothetically be visualized by US. However, the lack of plantar erosions seen on US suggests i) US may have a smaller-than-expected field-of-view, ii) the cortical bone is not clearly broken or iii) the size of the cortical break may be too small to see. Erosions visualized on US were often grade ≥ 2 on MRI. However, this early RA cohort had few such erosions.

10

Diagnostic Ascertainment of Axial Spondyloarthritis in Patients Presenting with Undiagnosed Back Pain: What is the Impact of MRI in Rheumatological Practice?

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Objectives: In current rheumatology practice, the circumstances that prompt clinicians to order MRI in patients with suspected axSpA are unclear and the degree to which MRI changes diagnostic ascertainment of axSpA in patients presenting with undiagnosed back pain has not been formally studied. We aimed to determine whether any particular patient characteristic(s) is associated with rheumatologist ordering of MRI and to assess the impact of MRI evaluation on diagnostic ascertainment of axial SpA in patients presenting with undiagnosed back pain.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA. Consecutive patients ≤ 45 years of age with undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. Differences in patient characteristics between those who did or did not have MRI examination were assessed by chi-square and t-tests. We also assessed the degree of diagnostic reclassification after each step.

Results: 225 patients (52.0% male, mean age 34.7 years, mean age at symptom onset 27.5 years, B27+ 35.1%) were referred with AAU (30.7%), psoriasis (20.4%), Crohn's colitis (34.2%), ulcerative colitis (19.1%). A diagnosis of axSpA was made in 66.7% of patients after stage 1 clinical evaluation and in 55.8% in stage 2 after review of the labs and radiography.

Radiographic sacroiliitis according to modified New York criteria (mNY) was reported in 30.7% according to local site reads. MRI evaluation was conducted in 129 patients and was ordered significantly more frequently when radiography was mNY- (76.7% vs 57.8%, $p=0.004$) and in those without Crohn's colitis (71.3% vs 51.8%, $p=0.004$). After review of the MRI scan at stage 3, diagnostic categorization of axSpA decreased from 55.8% to 46.6%, 21 (17.8%) patients being recategorized from SpA to non-SpA and 4 (3.4%) from non-SpA to SpA. Confidence in diagnostic categorization was increased after MRI.

Conclusion: In a setting of undiagnosed back pain and higher risk for axial SpA, use of MRI is primarily driven by negative radiography. MRI was primarily helpful in ruling out SpA and reducing false positives.

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Physician Global Assessments for Disease Activity in Rheumatoid Arthritis are all over the Map! Results from a CRA Survey

Matthew Turk (Schulich School of Medicine & Dentistry, UWO, London); Janet Pope (Western University, Department of Medicine, Division of Rheumatology, London)

Objectives: A physician (MD) global assessment is part of routine care in monitoring patients with rheumatoid arthritis (RA) and in clinical trials and it is part of some composite measures (CDAI, SDAI). However, the variability between physicians with respect to their global ratings is not known. We wanted to determine the variability of MD global assessments in RA and if results varied between rheumatologists based on their age, sex, practice setting, experience (number of patients seen per year), and years in practice.

Methods: Our research goal was to determine the variability of MD globals and which factors are associated with discrepancies. We surveyed rheumatologists who were members of the Canadian Rheumatology Association using RA patient scenarios where each was rated for disease activity from 0 – 10. Cases were developed to span the spectrum of disease activity. Means, t tests, correlations and Fleiss' Kappa statistics were used to analyze the responses.

Results: A total of 145 responded to the survey (40% response). MD globals were not significantly different between physicians in any demographic category. The range of answers for the same scenario was as high as 7.6 out of a possible 10, indicating vast discrepancies between physicians. Some scenarios outlined changes in individual patients, however physicians surveyed were often in disagreement as to how much the patient recovered or worsened but the direction was the same (i.e. if better all agreed). The average range for their answers was 7 out of

a possible 10 with a mean standard deviation of each answer was 1.7. The average Q1-Q3 interquartile range was 3 and overall Fleiss Kappa was 1.16×10^{-3} (indicating poor to slight agreement for many case scenarios). Mean kappa for new questions was 1.16×10^{-3} , whereas for change scenarios it was 2.513×10^{-3} (only slightly numerically better for changes in diseases activity).

Conclusion: This research emphasizes the need to establish evaluation criteria in RA for disease. Perhaps a catalogue of patient scenarios that range from 0 to 10 could be developed, standardized and agreed upon to decrease the wide variability of ranking by rheumatologists.

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Pregnancy Outcomes in Patients with Childhood-onset Systemic Lupus Erythematosus

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Objectives: The literature suggests that patients with childhood-onset systemic lupus erythematosus (cSLE) have more severe disease than those with adult-onset, and that SLE can impact pregnancy outcomes. Hence cSLE patients with severe disease may be at risk for poor pregnancy outcomes. The purpose of this study is to describe pregnancy outcomes in cSLE patients.

Methods: A retrospective chart review was conducted of patients with cSLE (disease onset ≤ 18 years), followed at the Lupus Clinic at the Hospital for Sick Children (HSC) in Toronto. Of those, we identified patients who had at least one pregnancy, through cross-referencing OHIP numbers of patients seen at the HSC Lupus Clinic and by one of the two specialists in pregnancy in the rheumatic diseases in Toronto, between January 1, 2007 and April 1, 2017. We assumed most cSLE patients would see one of these physicians in pregnancy. Pregnancy and SLE data were abstracted using a standardized form. Variables included age at diagnosis, autoantibody profile, including antiphospholipid antibodies (APLAs) and/or antiphospholipid syndrome, renal involvement, and SLE treatment. Obstetric information included pregnancy outcome and complications. Proportions of patients with features and outcomes were calculated using Microsoft Excel software.

Results: There were 56 pregnancies in 24 patients from the cSLE cohort of 646 female patients, most of whom were of post-pubertal age between 2007 and 2017, who fulfilled an average of 6 ACR and 7 SLICC criteria for lupus. The mean age at diagnosis of SLE was 14 (10-17) years and mean age at pregnancy was 29 (21-40) years. Of 56 pregnancies, 16 were term (28.6%), 16 preterm (28.6%), 12 miscarried (21.4%), 9 therapeutically terminated (16.7%), and 3 stillborn (5.5%). 5/24 (21%) patients had preeclampsia. Fifty percent (12/24) had SLE renal involvement; the majority (10) had proliferative (class III/IV) nephritis. Fifty percent (12/24) had APLAs. Of these, 2/12 (17%) experienced thrombosis prior to pregnancy.

Conclusion: There were strikingly few pregnancies documented. The pregnancies were complicated, and had worse outcomes than those previously described for adult-onset cohorts. The patients had high rates of nephritis and APLAs, consistent with previous reports of cSLE.

These findings could reflect uniquely poor pregnancy outcomes in cSLE, or a skewed sample of patients with more severe disease who, consequently, continued to be followed in tertiary care. We will attempt to expand this cohort by contacting all female HSC cSLE patients to document additional pregnancies and explore predictors for outcomes in this population. Best Abstract on SLE Research by a Trainee - Ian Watson Award

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Quantification of Leukocytes' Secretome to Guide Diagnosis and Treatment Options in Patients with Suspected Chronic Auto-Inflammatory Syndromes

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Objectives: Auto-inflammatory syndromes are inherited conditions characterized by recurrent inflammation (fever, abdominal pain, dermatitis, arthritis). Diagnosis and treatments are challenging as detection rate of mutations in patients with high suspicions for auto-inflammatory syndromes is low, symptoms are reminiscent of other autoimmune diseases, especially Systemic Autoimmune Rheumatic Diseases (SARD), and the cytokines abnormally secreted are unknown. As a consequence, patients can be misdiagnosed, leading to inappropriate treatment, severe complications and substantial socio-economic costs, as AIS often severely affect young children, impeding their education and subsequent employability. Since auto-inflammatory syndromes are characterized by abnormal secretion of cytokines, our objectives were to quantify the cytokines in the plasma and the cytokines secreted (secretome) by in vitro-activated peripheral blood mononuclear cells (PBMCs) to distinguish suspected auto-inflammatory syndrome patients from SARD patients and healthy individuals, and provide personalized biotherapy options.

Methods: Plasma and PBMCs were obtained from healthy controls, suspected auto-inflammatory patients, and definite rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients from the CHU de Québec SARD Biobank Repository Database (SBRD). PBMCs were stimulated with inflammatory and immune stimuli, and nine cytokines (IL-1 α , IL-1 β , IL-1RA, IL-18, IFN γ , IL-12, TNF, IL-6 and CXCL10/IP-10) were analyzed by multiplex assays in the plasma and cell supernatants.

Results: The cytokines found in the plasma of suspected auto-inflammatory patients were not different between both healthy donors and definite SARD patients. In contrast, PBMCs had a distinct profile of cytokine secretion. Stimulation of PBMCs with IL-15 or anti-immunoglobulins led to differential secretion of members of IL-1 cytokine family, IL-12 and IFN γ in definite SARD, but not auto-inflammatory patients. Moreover, suspected auto-inflammatory patients can be distinguished from healthy donors and definite SARD patients by quantification of IL-12, IL-1 α and IL-18 levels in leukocytes' supernatant following distinct inflammasome activation. Stimulation with inflammasome activators or pro-

inflammatory cytokines led to selective secretion of IL-1 α , IL-1 β , IL-1RA, IL-18, IFN γ or IL-12 in suspected auto-inflammatory patients that can be targeted by biotherapies.

Conclusion: This study demonstrates that analysis of leukocytes' secretome is reliably more sensitive than plasma to reveal cytokine signatures and to predict treatment options in patients with suspected chronic auto-inflammatory syndromes.

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Risk of Major Congenital Malformations Associated with Exposure to Biologics Before or During Pregnancy: A Population-based Cohort Study

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Objectives: As most biologics cross the placenta during human pregnancies, there remains concern whether in-utero exposure may be associated with increased risk of major congenital malformations (MCM). A recent meta-analysis found a non-statistically significant trend towards increased risk of MCM, however most of the published studies have not adjusted for differences in disease activity between exposure groups. Our objective was to evaluate the association between biologics exposure and risk of MCM by applying high dimensional propensity scores (HDPS) in population-based administrative data.

Methods: We conducted a population-based, retrospective cohort study using British Columbia administrative data including all physician visits, hospital admissions, and dispensed medications, linked to a Provincial Perinatal Registry. Our cohort included women with autoimmune disease who had ≥ 1 pregnancies, and infants born to these women, between 01/01/2002 and 12/31/2012. Pregnancies were defined as exposed if women had at least one biologic prescription 90 days before pregnancy or up to 13 weeks gestation (first trimester), and unexposed if there were no prescriptions for biologics during the same period. Each exposed pregnancy was matched with 5 unexposed pregnancies using HDPS. The outcome of interest was defined as the occurrence of ≥ 1 MCMs identified at birth. Logistic regression models were used to evaluate the association between exposure to biologics and risk of MCMs in the HDPS-matched cohort. Sensitivity analysis was conducted using multivariable logistic regression models with deciles of HDPS.

Results: The cohort included 131 pregnancies (120 women) exposed to biologics 90 days before pregnancy or during the first trimester, and 599 HDPS-matched pregnancies (578 women) that were not exposed to biologics during that time. In the exposed group, 94% had prescriptions for infliximab, etanercept, or adalimumab. In the exposed and unexposed groups, respectively, 10/131 (8%) and 40/599 (7%) of newborns had ≥ 1 MCMs at birth. In the unmatched cohort, the odds ratio for those exposed to biologics was 1.46 (95% confidence interval [CI] 0.78-2.72) compared to unexposed, whereas in the matched cohort it was 1.16 (95% CI 0.56-2.37), suggesting no association between biologics exposure and MCM. Sensitivity analyses did not materially change our results.

Conclusion: These population-based data suggest that use of biologics before pregnancy or during the first trimester may not be associated with MCM in infants born to women with autoimmune inflammatory diseases. Given the effectiveness of biologics in controlling disease

activity, findings emphasize the importance of balancing benefits and risks of treatments for patients who may be pregnant or considering pregnancy.