1

A Progressive Increase in T follicular Helper Cells Marks the Transition from Benign to Symptomatic Autoimmunity

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Objectives: The systemic autoimmune rheumatic diseases (SARD; Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Sjogren's Disease (SjD), Systemic Sclerosis (SSc)) are characterized by prolonged pre-clinical autoimmunity, culminating in clinical disease. Evidence from disease-specific studies (e.g., SLE and RA) suggests that this pre-clinical phase is marked by accumulation of pathogenic auto-antibodies (auto-Ab). The cellular derangements that promote auto-Ab production are unknown. T follicular helper (TFH) cells drive plasma cell differentiation and immunoglobulin production and are implicated in the development of autoimmunity. TFH expansion is seen in patients with established SARD but has not been defined in patients with pre-clinical SARD autoimmunity. We examined the relationship between TFH and auto-Abs in ANA positive individuals prior to the development of SARD.

Methods: ANA+ (titer $\geq$ 1:160) patients (n = 63) were recruited from a tertiary care rheumatology center. Healthy controls (n = 27) with no history of autoimmunity were recruited. Patients were stratified into clinical groups; (1) no defining SARD symptoms (n = 19), (2) undifferentiated connective tissue disease (UCTD, n = 12); one or more SARD defining symptom, (3) SARD (n = 32); fulfilling ACR criteria for a diagnosis of SLE, SjD, RA or SSc. Patients were steroid and DMARD naïve. PBMCs were isolated over a Ficoll gradient, stained with combinations of fluorescently-labeled antibodies and analyzed by flow cytometry. The extractable nuclear antigen auto-Ab profile (anti-Ro, -La, -Sm, -RNP, -Scl-70, -centromere) was determined. Mann-Whitney non-parametric testing was used to compare groups with $p < 0.05$ indicating a statistically significant difference.

Results: The proportion of TFH (CD4+, CXCR5high, PD-1high) cells was significantly elevated ($p = 0.04$) in patients vs controls. UCTD patients had a significant expansion in TFH cells when compared to asymptomatic ANA+ individuals ($p = 0.009$). SARD patients (vs UCTD) showed a non-significant trend to increased proportions of TFH. Patients (n = 45) with higher ANA titers ($\geq$ 1:640) had a statistically significant increase ($p = 0.01$) in TFH compared to individuals (n = 9) with lower ANA levels (1:160). Linear regression analysis showed a positive correlation ($p < 0.0001$) between the proportion of TFH and the number of auto-Abs in patients.

Conclusion: In ANA+ individuals, expansion of TFH cells was associated with the accrual of auto-Abs and the development of clinical symptoms, suggesting that dysregulation of this cellular compartment contributes to the progression towards clinically significant autoimmunity. This identifies TFH cells as a potential target for therapeutic intervention to prevent the development of SARD.

2

Interrupted and Delayed Care in First Nation Patients with Rheumatoid Arthritis: The Best Target for Therapy?

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Objectives: Severe disease and poor outcomes have been described in First Nation (FN) patients with Rheumatoid Arthritis (RA). We examined the contributions of interrupted and delayed care to the outcomes of FN RA patients compared with Caucasian (CA) patients with RA.

Methods: Our academic centre maintains a prospective database that includes demographics, year of disease onset, and date of first and subsequent clinic visits, and ethnicity. At each visit, patients complete a modified health assessment score (mHAQ), disease activity visual analogue scales (VAS), physicians complete joint counts, physician global VAS, a Lansbury Index (LBI), and current treatment information. After excluding patients if disease duration was >15 or <1 year, or if there were <2 clinic visits, records of the most recently assessed 150 FN and 150 CA RA patients were abstracted. The database was supplemented with the provincial electronic imaging and laboratory databases for each patient, to determine serology, acute phase reactants, and radiologic damage or documented joint deformities.

Results: Records of 154 CA and 150 FN patients were abstracted. Disease duration and gender were similar in CA compared to FN (9±4 vs 8±5 years; and 79% vs. 85% female respectively). 35% of FN lived >500 km away compared to 1% of CA ($p<0.001$). FN patients were younger at disease onset than CA, (40±13 vs 49±17 years; $p<0.001$). At clinical presentation, FN were more likely to be seropositive for both RF and ACPA compared to CA, (59% vs 46%;$p=0.02$) and had higher ACPA titres (114±88 vs 68±82;$p<0.001$) The two groups did not differ in mHAQ, ESR, CRP, VAS, tender, or swollen joint counts at first visit, but FN had higher LBI scores (40±36 vs 28±33; $p=0.012$). FN had more total DMARD trials over their disease course (5.1±3.2 vs 3.7±2.5; $p=<0.001$), and were off DMARD therapy for longer periods in total (36 months ±30 vs 25±40; $p=0.009$), had fewer clinic visits/year (5±12 vs 3±7; $p=0.072$). At the last visit, FN had higher mHAQ scores (.71±47 vs .42±52; $p<0.001$), higher LBI (34±37 vs 20±30;$p=0.003$), and more frequent joint damage/deformity, (85% vs 74%;$p=0.02$).

Conclusion: The younger onset age, more frequent seropositivity, and higher LBI suggest biologically more severe disease, but our data suggests differential care delivery with modifiable factors over the disease course that likely impact outcomes, including treatment delays, missed appointments, and interrupted treatment. Improved care delivery models, particularly incorporating outreach care, have the potential to improve outcomes substantially for this population.

3

Positive Spine MRI for Inflammation Predicts Radiographic Progression in Patients with Ankylosing Spondylitis

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Objectives: Inflammation at vertebral corners on MRI has been shown to predict development of syndesmophytes in patients with AS. However, it is unclear at a patient level whether a positive spine MRI for inflammation identifies patients at higher risk for radiographic

progression and whether this is also associated with the degree of spinal inflammation. We used the SPARCC MRI spine score to assess whether the proposed cut-off of ≥2 for positive spine MRI and the absolute score are predictive of radiographic progression.
Methods: Spinal inflammation was scored blinded to time point (baseline, 2 years) using the SPARCC spine score by two readers and an adjudicator using pre-specified rules for adjudication. MRI scans were assessed from a prospective cohort of 195 AS patients (mean age 40.3 years, mean symptom duration 16.6 years, 59% on anti-TNF) followed for mean 2.3 years. Two readers and an adjudicator independently scored pairs of radiographs (baseline, 2 years) from the same patients using the mSASSS. Radiographic progression was compared in patients with and without positive spine MRI (SPARCC ≥2 or <2) and the degree of spinal inflammation at baseline (absolute SPARCC score) was compared in patients with and without radiographic progression (mSASSS >0 or =0) using Mann-Whitney and cumulative probability. Multivariate regression analyses included variables significant in univariate analyses (age, sex, symptom duration, CRP, baseline mSASSS) and treatment.
Results: Radiographic progression was significantly greater in those with positive spine MRI (p=0.004), and especially in patients who only received non-biologic therapy (p=0.006). Baseline SPARCC spine inflammation scores were significantly higher in those who developed radiographic progression compared to those without (14.5 vs 8.7, p=0.002). Positive spine MRI and the degree of spinal inflammation score were both significantly associated with radiographic progression in multivariate analysis (β=0.26 (p=0.019) and β=0.006 (p=0.036), respectively).
Conclusion: Both a positive spine MRI for inflammation and the degree of spinal inflammation are significantly associated with radiographic progression in patients with AS.

4

Rheumatologist Care in Rheumatoid Arthritis: Are we dropping the Ball?

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Objectives: Our objective was to evaluate the persistence of rheumatologist care over time and the impact on DMARD use in a population-based incident cohort of RA for the province of British Columbia.
Methods: We conducted a retrospective cohort study using administrative health data among all incident RA cases identified between Jan 1997 and Mar 2006 followed until Dec 2010, using previously described RA criteria. Cases were selected for this study if they had at least two rheumatologist visits with RA diagnoses. Cases were followed from their first rheumatologist visit at or after cohort index date until their last health care utilization, when they were censored and removed from the denominator for calculating DMARD use or rheumatologist care rates. Rheumatologist care and DMARD use per year were defined as having at least one rheumatologist visit, or one DMARD prescription, within 365 days of the anniversary of the first rheumatologist visit. Rates of DMARD use were measured according to pattern of rheumatologist care. Confidence intervals for proportions were constructed using the normal approximation.
Results: The sample included 9,224 RA cases (71.5% female; mean[SD] age 56.7[16.0] years; median follow-up 6.7 [IQR 4.9;9.1] years). Lack of continued rheumatologist care was frequent and was associated with lower rates of DMARD use. In the sixth year of follow-up, only 34.4% had seen a rheumatologist yearly for the preceding 5 years; and only 30.8% had at

year 9. At year 6, 13.9% had not seen a rheumatologist in the preceding 5 years, and this rate increased to 18.8%, 22.8% and 24.7% at years 7, 8 and 9, respectively. At year 6, the rate of DMARD use was 91.5% [95%CI:90.4;92.6] for those with continuous rheumatologist care over the prior 5 years, and 22.7% [95%CI:20.1;25.4] for those without any rheumatologist care in the preceding 5 years. Those without rheumatologist care for the preceding 4, 3, 2 and 1 year had rates of DMARD use of 36.6%, 36.7%, 45.4%, and 61.1%, respectively. Over all years of follow-up, those who stopped seeing a rheumatologist had decreasing yearly rates of DMARD use while off rheumatologist care, and those who subsequently returned to rheumatologist care had a gradual increase after resuming rheumatologist care.
Conclusion: Our results suggest that, in British Columbia, RA patients frequently stop seeing their rheumatologist and this has a negative impact on DMARD use. This has implications for planning models of care in view of increasing demands on rheumatologist's manpower.

5

The Association of Type I Interferon and Disease Activity in Childhood-Onset Systemic Lupus Erythematosus (cSLE)

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Objectives: The objectives of our study were to determine the type I IFN signature by measuring the expression levels of five IFN-inducible genes (IFIGs), and to correlate IFN score with disease activity and clinical features in cSLE.
Methods: Type I IFN signature was assayed by exposing HeLa cells to sera from 132 cSLE patients and 29 healthy controls using a previously validated bioassay. Five IFIGs (MX-1, C1orf-29, IFIT1, PRKR, and IFI44) were quantified by real-time PCR. Following data normalization, an IFN score was calculated by summing the relative expression levels of the IFIGs. Data collected included clinical features (ACR classification criteria), SLEDAI-2K at sample collection and since diagnosis (adjusted mean SLEDAI), serological markers (ESR, C3, and C4), autoantibodies at the time of IFN testing (anti-dsDNA, anti-Smith, anti-RNP, anti-Ro, anti-La, and anti-cardiolipin), and cumulative glucocorticoid exposure 3 and 6 months preceding sample collection. Mann-Whitney and Kruskal-Wallis tests were used as appropriate while for the IFN score t-test, ANOVA and Pearson correlations were used as appropriate.
Results: The study included 109 female and 23 male cSLE patients (38.6% Asian, 29.5% Caucasian, 16.7% African-American, 4.5% Hispanics, 0.8% Aboriginal, and 9.8% mixed) with a median (IQR) age of 15.4 (13.1, 16.9) years and median (IQR) disease duration of 16.2 (7.8, 33.5) months. Patients with longer (>2 years) disease duration had higher IFN scores than those with shorter (≤1 year) disease duration ($p=0.034$). IFN scores did not differ between genders ($p=0.780$) or among different ethnicity groups ($p=0.411$). The expression levels of MX1 ($p<0.001$), C1or29 ($p=0.009$), PRKR ($p<0.001$), and IFIT44 ($p=0.037$) but not IFIT1 ($p=0.260$) were significantly increased compared to the controls. The median IFN score was significantly higher in patients with serositis (10.2 vs. 6.4; $p=0.045$) and was significantly lower in patients with malar rash (6.1 vs. 8.4; $p=0.039$). IFN score was associated with the number of autoantibodies ($p=0.034$), as well as with cumulative glucocorticoid dose over 3 (rho= –0.18 and $p=0.038$) and 6 (rho= –0.17 and $p=0.040$) months prior to sample collection. However, IFN score was not associated with SLEDAI-2K, serological markers, or the SLE classification criteria.

Conclusion: The associations of upregulated IFN signature with disease activity as well as renal and/or neurologic involvement reported in aSLE were not seen in this cohort of cSLE. The lack of associations may represent an intrinsic difference between aSLE and cSLE and suggests differing disease mechanisms.

6

The Risk of Growth Retardation and Obesity in Children with Juvenile Idiopathic Arthritis (JIA) Treated with Contemporary Treatments: Results from the ReACCh-OUT Cohort

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Objectives: Background: Children with JIA are at risk for obesity and growth retardation due to active disease and use of corticosteroids. With current treatments, most children with JIA attain inactive disease within 2 years. It is unknown whether these improved outcomes translate to improved growth, or lower risk of obesity. Objective: To estimate the risk of growth retardation and obesity in a prospective inception cohort of children with JIA.

Methods: 1154 children with newly diagnosed JIA at 16 Canadian Centres between 2005 and 2010 were included. Height and weight measurements at 0, 6, 12, 18, 24, 36, 48 and 60 months after enrolment were used to calculate changes in age and sex standardized scores (z-scores) for height, weight and BMI over time for each JIA category using Canadian Paediatric Endocrinology Group normal reference values. Growth retardation was defined as a drop of 1.0 z-scores or more in height, relative to baseline. Obesity was defined as an increase of BMI above the 95th percentile for age and sex. Kaplan Meier survival methods were used to estimate the risk of growth retardation and obesity.

Results: The median age at diagnosis was 9.5 years (4 to 13) and 64% were female. The median follow-up was 35.5 months (IQR 22.9 to 48.8). At enrolment, the z score for height was 0 (IQR -0.71 to +0.82) and the z score for weight was 0.30 (-0.39 to +1.1), compatible with normal height and some overweight at baseline. The risk of growth retardation at least once within the first 3 years after diagnosis was 8.9% (95%CI = 7.1 – 11). The risk varied from 5.9% (2.8 – 12.4) in children with enthesitis-related arthritis to 24.4% (15.3 – 37.5) in children with systemic JIA. Overall, 16.8% of children were obese at enrolment. The risk of becoming obese during the first 3 years after diagnosis was 10.5% (8.6 – 12.9). It varied from 9.4% (5.3 – 16.6) in children with enthesitis-related arthritis to 34.7% (23.2 – 49.9) in children with systemic JIA. Systemic corticosteroids were prescribed for 85.5% of children with systemic JIA. A dose of 1mg/Kg of prednisone corresponded to a decrease of 0.48 in z score for height and an increase of 0.45 in z score for BMI.

Conclusion: Despite advances in treatment, children with JIA still have a considerable risk of growth retardation and obesity, particularly if they have systemic JIA and have received systemic corticosteroids.

7

Treatment Preferences of Patients with Early Rheumatoid Arthritis: A Discrete-Choice Experiment

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Objectives: To determine the preferences of patients with early RA amongst factors relevant to evidence-informed discussion of DMARD treatment options.

Methods: A computer-based (in clinic or at home) cross-sectional survey using a discrete-choice experiment was performed in consecutive adult patients with early RA (<2 years since diagnosis) in 2 Canadian centres. Patients were asked to choose between 3 hypothetical DMARD choices, described by 8 attributes, each with a set of different levels. The attributes were those determined to be most relevant to an evidence-informed shared discussion of usual DMARD treatment options using a nominal-group technique with a panel of 5 experts. From participants' survey choices, the part-worth utility of each level was estimated using a hierarchical Bayesian regression model and scaled from -10 (strong aversion) to +10 (strong preference). The relative importances (range of utility values across all levels) of attributes were compared. Preference heterogeneity was explored using latent class analysis.

Results: 152 of 187 eligible patients (81%) completed the survey: mean age 52, 63% female, disease duration 7.8 months. Fourteen (9%) were DMARD naïve, and 44% had changed DMARD treatment within 3 months. The chance of a major symptom improvement by 6 months (range 30%-70%) was the most important attribute, followed by the chance of developing serious joint damage by 10 years (range 2%-30%). Patients had an aversion to IV therapy (utility -7.3), but were relatively indifferent to other dosing regimens: weekly pills (utility 2.0); weekly injections (utility 1.2); weekly + 6 daily pills ('triple therapy') (utility 0.45). Of potential adverse events, a 'small risk of serious infections/possible risk of malignancy' was the most important (utility -3.6), but patients were willing to accept this risk, on average, for a 6% absolute increase in the chance of a major symptom improvement. The chance of having a nuisance side effect requiring treatment discontinuation and a rare risk of lung/liver disease with need for regular bloodwork were less important. Alcohol restriction and the need to have regular eye exams to screen for eye toxicity were unimportant. Latent class analysis revealed a group of patients that were more risk averse, particularly to a potential risk of serious infection/malignancy; no patient characteristic accurately predicted classification to this group.

Conclusion: Patients with early RA are focused on treatment benefits and are generally willing to accept multiple medications, subcutaneous delivery, and a risk of minor non-serious or rare serious side effects for a small increase in the chance of benefit.

8

Developing System Level Performance Measures for Evaluating Models of Care for Inflammatory Arthritis

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Health Academy, Edmonton); Heidi Tibollo (Doctor Evidence LLC, Santa Monica); Sean Grant (The RAND Corporation, Santa Monica); Khodyakov Dmitry (The RAND Corporation, Santa Monica); Diane Lacaille (University of British Columbia/ Arthritis Research Centre of Canada, Richmond); Lori Tucker (BC Children's Hospital, Vancouver)
Objectives: The Arthritis Alliance of Canada (AAC) represents 36 member organizations with the mandate of improving arthritis care in Canada. Previous AAC work includes the development of pan-Canadian models for inflammatory arthritis (IA) care. The purpose of this study is to develop a set of system level performance measures for model evaluation and continuous improvement for IA care in Canada. IA is defined as: rheumatoid arthritis (RA), ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis.
Methods: A scoping review of measures and guidelines for IA care was conducted and a set of 25 measurement themes was presented to a working group of arthritis stakeholders. The measurement themes were discussed and expanded upon and 34 measurement themes were derived following the meeting. An iterative process was used to define 16 candidate measures and measures not in scope or overlapping were discarded. The 16 measures were submitted to 13 AAC members in an online poll to rank the measures and rate the following three criteria on a 1-9 scale: relevance to arthritis care, how likely the measure was to be important for system improvement and how feasible it was to obtain data for measurement. The top seven were presented at an AAC stakeholder meeting to clinicians, health policy makers, managers, allied health professionals and patient advocates and further stakeholder input was obtained. One outcome measure on disease activity in RA was excluded due to feasibility concerns. A set of six performance measures was defined and supported by a systematic review of guidelines and existing measures. Fifty-one arthritis stakeholders including patients, rheumatologists, allied health professionals and researchers have evaluated and discussed the measures using an online modified Delphi process.
Results: Six measures have been selected for inclusion in the set: Waiting times for rheumatology consultation for patients with new onset IA, percentage of IA patients seen by a rheumatologist, percentage of IA patients seen in yearly follow-up by a rheumatologist, percentage of RA patients treated with a disease modifying anti-rheumatic drug (DMARD), time to DMARD therapy in RA and number of rheumatologists per capita. Outcome measures (e.g. disease activity) were excluded from the final set due to concerns about feasibility of measurement.
Conclusion: The first set of performance measures for IA care in Canada has been developed with broad stakeholder input. The measures focus on access to IA care, treatment and specialist resources and will inform continuous quality improvement for patients with for IA care across Canada.

9

Femoroacetabular Impingement (FAI) in Indigenous Populations: Prevalence, Physical Functioning, Quality of Life, and Health Care Utilization

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Objectives: FAI has recently emerged as a leading cause of primary osteoarthritis (OA). Little is known about the prevalence and impact of OA in Indigenous populations, and even less is known about FAI in this group. Thus, the aims of this study were: 1) to determine the prevalence of FAI and hip pain in Indigenous populations in British Columbia, and, 2) to characterize the association between FAI and hip pain and physical functioning, quality of life, and health resource utilization in this population.
Methods: 90 individuals from member nations served by the Kwakiutl District Council Health Centres in North Vancouver Island enrolled in the present study. Eligibility criteria in addition to residence included age between 20 and 49 and availability for an onsite physical assessment, x-ray, and questionnaire administration. Participants were asked if they had any pain, stiffness or discomfort in the groin or the front of the upper thigh (i.e., hip pain) in the past 12 months. Plain radiographs were taken in 3 views and evaluated by a trained musculoskeletal radiologist using a standardized protocol to identify cam (alpha angle>55°) and pincer (focal acetabular retroversion, or lateral centre edge angle >40°) impingement. Physical functioning, life quality, and health resource utilization were recorded by assessor-administered questionnaires. Data analysis was carried out using SAS 9.4 statistical software.
Results: The prevalence of FAI in this Indigenous population was 23.5% (95% CI: 14.5%, 32.5%) while hip pain prevalence was 29.3% (95% CI: 19.9%, 38.8%). Hip Osteoarthritis Outcome Scores (HOOS), which assess physical functioning and life quality were not significantly different between those with and without radiographic FAI. However, HOOS scores were significantly lower in those with hip pain compared to those without hip pain. General practitioner visits occurred at a rate of 54.3% in the study population and this rate did not significantly differ in those with or without radiographic FAI or hip pain. Similarly, there was no difference in difficulty experienced at work/volunteer or leisure activities between groups.
Conclusion: The prevalence of FAI was lower than expected given the high prevalence of OA among Indigenous populations, illustrating the complex nature and need to better characterize the interaction between FAI and the development of hip OA and symptoms. Hip pain was prevalent and was associated with a decreased level of physical functioning and life quality. Despite this, there was no increase in general practitioner utilization warranting further investigation into potential barriers to medical care in this population.

10

Elevated 14-3-3η Serum Protein Levels Increase RA Confirmation in Recent-Onset Polyarthritis Patients

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Objectives: To determine if 14-3-3η serum levels are additive to available RA-associated autoantibodies to identify Rheumatoid Arthritis patients in a cohort of recent-onset polyarthritis cohort.

Methods: Using the Augurex ELISA, serum 14-3-3η levels were measured at baseline in 332 patients with recent-onset polyarthritis (EPA) from the Sherbrooke EUPA cohort, for which a follow up of at least 5 years was completed. Patients were rapidly and intensively treated with DMARDs and/or biologics to achieve clinical remission defined as 0 swollen joints among 66. For 14-3-3η measurements, the manufacturer's (Augurex 14-3-3η ELISA) reported diagnostic cut-off of ≥0.19 ng/ml was used. Anti-CCP2 (EuroImmun and QuantaLite, Inova Diagnostics) and IgM Rheumatoid Factor (RapiTex, Dade-Behring) were determined using commercial assays and Anti-Sa, using an in-house assay previously described (Boire G et al. 2005. Arthritis Research & Therapy, 7:R592-R603).
Results: Median age of the 332 patients was 60 years and 62% were female; median time of symptom duration was 4 months at inclusion. Up to 98.7% were treated with DMARDs between baseline and the 18-month follow up; 24 also received biologic agents over the first 18 months. 14-3-3η was positive at baseline in 45.7% of patients and RF, ACPA and anti-Sa were positive respectively in 146 (44%), 132 (39.9%) and 73 (22%) of patients. When 14-3-3η was combined with other antibodies, the proportion of patients with at least one positive test increased to 54.8% (RF or 14-3-3η), 55% (anti-CCP2 or 14-3-3η) and 49.7% (anti-Sa or 14-3-3η), corresponding to an incremental benefit in sensitivity of 25%, 38% and 126%, respectively. When RF, anti-CCP2 and anti-Sa were combined, the number (proportion) of positive patients for at least one marker amounted to 164 (51.0%); when 14-3-3η was added to the antibodies, the number (proportion) of positive patients for at least one marker increased to 194 (58.6%).
Conclusion: Serum 14-3-3η positive status in recent-onset polyarthritis adds significant sensitivity to currently available RA-associated antibodies. Since higher 14-3-3η titres are associated with an increased risk of joint damage progression, our data support measuring it in early inflammatory polyarthritis to assist with patient stratification.

11

High Mortality in Vulnerable Canadians with Systemic Lupus Erythematosus

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Objectives: Disparate health outcomes have been described for vulnerable population groups. Expanding on our previous work examining mortality in Indigenous (IND) systemic lupus erythematosus (SLE) patients, we describe mortality in vulnerable populations with SLE, including ethnic minorities, low income, rural residents and those with low educational attainment.
Methods: Patients from a single academic center were followed from 1990-2014 using a custom database. Variables included date of birth, diagnosis, education, diagnosis date, ethnicity, disease manifestations (ACR classification criteria (ACRc)), treatment and date of death. Records of all patients with a diagnosis of SLE were abstracted. For patients not seen in the last 2 years, updated vital status was obtained from provincial medical records. Proximity to care was calculated, neighborhood income was obtained from Statistics Canada. Ethnicity was categorized into IND, Caucasian (CA) and other (OM). Rate ratios (RR) for potential years of life lost (PYLL) were compared between ethnicities, income, proximity to care, and educational categories. Survival time was compared using Kaplan Meier and Cox proportional hazard models.

Results: A total of 882 patients with SLE were identified: 218(25%) IND, 553(62%) Caucasian, and 111(13%) OM. Twenty-seven percent had not completed high school (noHS), 178(20%) were in the lowest income category (LoInc), and 99 (11%) lived >500km from care (>500km), while 543(61%) lived within city limits (City). IND were overrepresented in noHS, LoInc and >500km categories. There were no differences in ACRc, treatment and damage between education, income and care proximity groups. Survival was significantly worse for IND, LoInc, noHS and >500 (data not shown). RR(95%CI) for PYLL was as follows: 2.5(2.3-2.7) for IND compared to CA; 0.9(0.8-1.0) for OM compared to CA; 1.8(1.6-2.1) for LoInc compared to the highest; 2.5 (2.3-2.7) for noHS compared to graduates; and 2.6(2.3-2.8) for >500km compared to City. In individual analyses, after adjustment for age, gender, diagnosis date, ACRc, nephritis, and damage, hazard ratio (HR)(95%CI) for risk of death was 2.3(1.6-3.3) for IND; 1.7(1.2-2.5) for LoInc; 2.3(1.5-3.6) for >500km; and 1.8(1.3-2.8) for noHS. However, when all variables were combined, only IND remained significant, with an adjusted HR of 1.7(1.0-2.9).
Conclusion: Low income, low education, IND, and distance from care increased the risk of death roughly twofold in our SLE patients; however IND ethnicity was the greatest independent contributor to the risk of death. Our study suggests income, education, and remote location all contribute to high mortality in IND SLE patients, but additional undetermined factors require exploration and attention.

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Successful Withdrawal and Discontinuation of Immunosuppressants in Lupus Patients: Outcomes and Predictors

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Objectives: To determine the number of successful withdrawals of IS and their predictors in the lupus cohort.
Methods: Analysis was conducted on all Pts seen in The Lupus Clinic, from 1987-2012, in whom IS was tapered and stopped. Pts who were in clinical remission and on prednisone (P) ≤7.5mg/day were included. Tapering start was defined as the date of the visit with a decrease ≥25% in IS dose. IS Stop was the day of IS discontinuation. Study end was the date of flare or last clinic visit following IS stop. Flare was defined as the introduction of new IS or increase of P dose. Flare was evaluated within the first 2 years from IS stop and at any time after IS stop. Kaplan-Meier curve was used to evaluate the time to flare after IS stop. Pts who flared after IS stop were compared to Pts who did not flare at the time of IS tapering start and IS stop. Univariate and multivariate analyses were used to predict flare in patients who discontinued IS.
Results: Of the 1678 lupus Pts, 973 were ever on IS, 179 had tapering attempts and 99 Pts stopped IS. At tapering start age was 40.4±13.1 and disease duration was 11.4±9.4 years. Of the 99 Pts, 25 flared within 2 years. The length of time from tapering start to IS stop was 1.8±1.8 years in the no flare and 0.9±0.9 years in the flare group; p 0.002. 46 of the 74 Pts who had not flared by 2 years had follow-up available beyond 2 years. 17 Pts experienced a flared after year 2. Using Kaplan-Meier curve for time to flare showed that at 1, 2, 3, 4 and 5 years, 17%, 30%, 46%, 49% and 51% patients respectively flared. The percentage of Pts on P at the time of IS stop was greater among those who flared, 52% vs. 30%; p 0.04. At the time of IS stop, the results

from the logistic regression showed that Pts off P are more likely not to flare; OR 2.99; 95% CI: 1.13, 7.89; p 0.03.
Conclusion: Within 2 years, successful stopping of IS was possible in about 75% of clinically stable Pts. Half were successful within 3 year and this proportion was stable up to 5 years. At the time of IS stop, Pts who discontinued IS slowly and who were off P were less likely to flare.

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The Influence of Time-Dependent Drug Exposures on Joint Replacements in Rheumatoid Arthritis Patients: Cross-Provincial Comparisons

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Objectives: To evaluate total joint replacement (TJR), and the influence of early exposure to disease-modifying anti-rheumatic drugs (DMARDs) on time to TJR, comparing incident rheumatoid arthritis (RA) populations from Ontario and Quebec. We hypothesized that early DMARD exposures, soon after RA diagnosis, are associated with longer time to TJR.
Methods: Using a standard protocol, we performed population-based cohort analyses on new-onset RA patients in Ontario and Quebec from 2000-2013. Incident RA patients were followed from cohort entry until their first TJR surgery, or were censored at death date, or the end of study period, whichever came first. We studied all recipients of public drug coverage representing all Ontario seniors ages 66 years and older, and in Quebec, all seniors plus any non-seniors without private drug insurance. Analyses were also confined to patients who were a "new user" for the drug of interest. We used Cox proportional hazards regression with time-dependent variables measuring duration of drug use (in the first year of follow-up), separately for methotrexate and other DMARDs, adjusting for baseline age, sex, urban vs. rural residence, socioeconomic status, risk factors for TJR such as prior joint surgeries, osteoarthritis (OA), comorbidities, past use of COXIBs, NSAIDs and steroids, and time-varying cumulative use of concomitant drug exposures (anti-TNF inhibitors, COXIBs, NSAIDs, systemic steroids) during follow-up, and time-varying number of physician visits. Adjusted hazard ratios (HRs) along with 95% confidence intervals (CIs) were estimated.
Results: Among 20,918 Ontario and 11,256 Quebec RA patients, 67.6% vs. 67.5% were female, the mean (SD) age was 74.9 (6.3) vs. 65.3 (14.5) years, and 51.0% vs. 30.6% had co-existing OA at baseline, respectively. During a median follow-up time of 4.6 years in Ontario and 4.5 years in Quebec, 2,201 and 928 TJRs occurred, respectively. The rate for first-time TJR was 2.0 per 100 person-years (PY) in Ontario and 1.8 per 100 PY in Quebec. In both provinces, the median time to a TJR was 3.2 years. In the multivariable analyses, greater exposure to methotrexate, and other DMARDs within the first year was associated with longer time to TJR in both settings.
Conclusion: Cumulative exposures to methotrexate and other DMARDs, soon after RA diagnosis, were associated with longer time to TJR in both Ontario and Quebec. Our coordinated approach across provincial data sources identified highly comparable and consistent findings.