Methods: A prospective cohort study was performed on 294 sites in 276 patients with functional loss due to RA scheduled to undergo primary elective surgery between October 2012 and September 2014. There were 99 sites in 96 patients (males: 10, females: 86) whose disease activity was REM or LDA just before surgery. In the REM/LDA group, the average age was 63 (29–82) years, and the average disease duration was 17 (2–60) years. The surgical site was the shoulder in 1 patient, elbow in 7, wrist in 21, hand in 24, hip in 5, knee in 10, ankle in 4, and forefoot in 27. The procedures performed included 38 alloarthroplasties, 41 arthroplasties without prosthesis, 19 arthrodesis, and 9 synovectomies. The patient-reported outcome (PRO) was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), Patient's General Health using visual analogue scale of 100 mm (Pt-GH), and the Disabilities of the Arm, Shoulder and Hand (DASH) for the upper extremity surgery. The Time Up &Go test (TUG) was administered for patients receiving lower extremity surgery. The disease activity was assessed based on the 28-joint Disease Activity Score using C reactive protein (DAS28-CRP). All of these items were investigated just before surgery (baseline) and again at 6 and 12 months after surgery.

Results: On the whole, the physical function (HAQ-DI, DASH, TUG), QOL (HAQ-DI, EQ-5D, Pt-GH), mental wellness (BDI-II, Pt-GH), and disease activity (DAS28-CRP)[1)] were significantly improved at 6 and 12 months after surgery compared to baseline ($p<0.01$). In the REM/LDA group, a significant improvement was noted in the physical function (DASH, TUG) and QOL (EQ-5D) at 6 and 12 months after surgery; however, we did not observe any significant changes in any other items (Table 1).

Table 1: Outcome of combination therapy with medication and orthopedic surgical intervention

		HAQ-DI	EQ-5D	BDI-II	Pt-GH mm	DASH (UE)	TUG (LE) sec	DAS28-CRP
Total n=276 (UE: n=151, LE: n=125)	baseline	1.08 (0.74)	0.69 (0.11)	13.0 (8.7)	39 (25)	43.8 (22.2)	13.0 (9.5)	3.1 (1.0)
	PO# 6mos.	1.00** (0.78)	0.74** (0.14)	11.7** (8.2)	26** (21)	37.3** (29.1)	10.5** (5.4)	2.4** (1.5)
	PO# 12mos	0.98** (0.78)	0.75** (0.14)	11.6** (8.5)	27** (21)	36.2** (23.0)	10.7** (7.0)	2.4** (0.8)
REM+LDA n=96 (UE: n=50, LE: n=46)	baseline	0.84 (0.63)	0.73 (0.13)	11.0 (8.1)	18 (18)	35.2 (20.9)	9.8 (3.2)	2.1 (0.4)
	PO# 6mos.	0.81 (0.67)	0.79** (0.15)	9.9 (7.7)	18 (16)	30.2** (18.9)	9.0** (2.6)	1.9** (0.6)
	PO# 12mos	0.83 (0.70)	0.79** (0.16)	10.1 (8.1)	18 (18)	29.9** (20.3)	9.0** (3.0)	1.9 (0.6)

Mean(SD), **: p<0.01 compared to baseline

Conclusions: Achieving REM or LDA is not the ultimate goal of treatment for patients with functional loss caused by structural damage. Further "wellness" can be achieved by surgical intervention. Intensive combination therapy with medication and orthopedic surgical intervention is effective in improving the QOL and mental health as well as the physical function. Such intervention can also ameliorate the disease activity.

References:

[1] Oh K, Ishikawa H, Abe A, et al. Effects of surgical intervention on disease activity of rheumatoid arthritis: cases of surgery for rheumatoid arthritis of the lower limbs treated with biologics. Mod Rheumatol. 2014;24(4):606–11.

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AB0220 THE PROMISE OF ULTRASOUND GUIDED MINIMALLY INVASIVE SYNOVIAL BIOPSIES IN THE UNITED STATES

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Background: Currently we are in the golden age of therapy for patients with rheumatoid arthritis (RA). However, currently there exists no available assay to predict the response to a particular therapy for an individual patient. Today, rheumatologists do not have information at han for therapeutic decisions. It is clear that the target organ in RA patients, i.e. the synovium, has the potential to unlock the secret for determining therapeutic response. Ideally, a sufficient synovial sample would be obtained from each patient to perform histology, sorting of individual cell populations and transcriptional analyses.

Objectives: Our goal is to establish a minimally invasive ultrasound guided synovial biopsy program in the United States to obtain synovial tissue for determining therapeutic response.

Methods: Rheumatologists from six Universities in the United States were trained in ultrasound guided minimally invasive synovial tissue biopsy procedures. Only patients with a grey scale synovitis score of 2 or greater were selected. A disposable semi-automatic-guillotine type biopsy needle (Quick-Core) was utilized for all patients and 25/26 patients had the biopsy performed on the wrist. Histology was performed on whole tissue. RNA was extracted from whole tissue and from FACS sorted macrophages in order for RNA sequencing (RNA-seq) analysis to be performed.

Results: Our group has already performed over 26 minimally invasive ultrasound guided synovial tissue biopsies on RA patients with active disease. We had minimal adverse effects and patients tolerated the procedure very well. At least 6–12 needle biopsies of synovial tissue were obtained via biopsy per patient. A minimum of 4 needle biopsies were placed in formalin and synovial lining was confirmed via histologic analyses. The remaining pieces were used to prepare libraries for RNA-seq. We observed comparable RNA integrity numbers, a measure of RNA quality, between the whole synovial tissue from RA (biopsy obtained) and OA (surgically-obtained) patients. OA patients segregated together transcriptionally, while RA patients are more heterogeneous as demonstrated via RNAseq analysis. We also optimized a protocol for digestion of synovial tissue biopsies for isolation of macrophages. We identified genes differentially associated with macrophage activity in RA versus OA synovial macrophages that were not evident in the whole tissue transcriptional profile.

Conclusions: Ultrasound guided synovial tissue biopsies are feasible in the United States. Based on our recent success using minimally invasive ultrasound guided synovial biopsies, we believe that this procedure coupled with cutting-edge technologies will provide the critical information to rheumatologists to establish precision based medicine as a reality for RA patients.

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AB0221 IMPACT OF SMALL TO MEDIUM DOSE OF PREDNISOLONE ON BONE MINERAL DENSITY AMONG EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent randomized trials in rheumatoid arthritis (RA) using low to medium dose of corticosteroid showed that bone mineral density (BMD) loss over 2 years was not significantly different from that with placebo. Another study in early RA and undifferentiated arthritis even showed a positive correlation between cumulative glucocorticoid (GC) dose with an increase in BMD at the ultradistal forearm. Whether the use of prednisolone (pred) can prevent bone loss in early RA patients remained controversial.

Objectives: The aim of this study was to investigate the impact of small dose pred (≤10mg/day) on BMD in early RA patients.

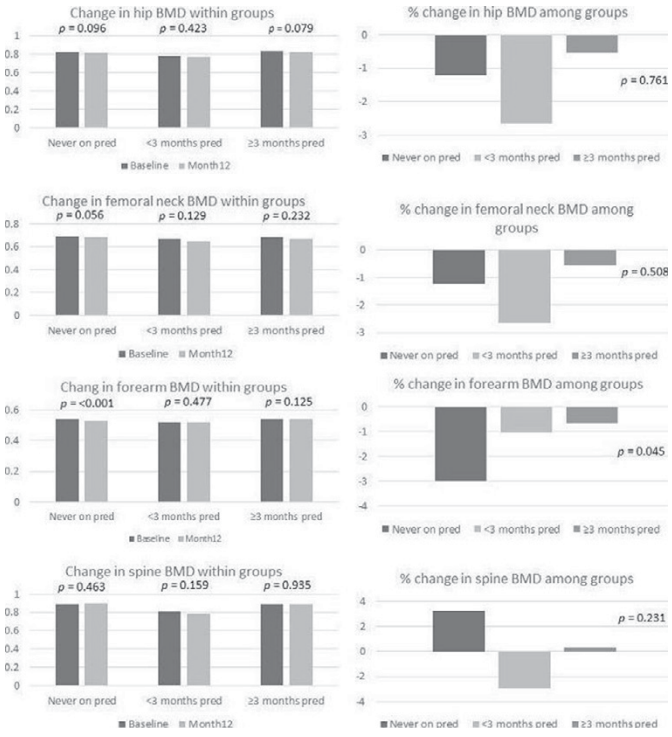
Methods: Data from 107 patients ((age: 53.3±11.92 years; females: 79 [73.8%], median disease duration at entry: 7-month (IQR, 4–12)) from the Hong Kong early arthritis registry (Clinical Rheumatology Systematic Treat to Target in Asia Leadership [CRYSTAL] project)were analyzed. In this register, clinical and treatment information were recorded systematically, including cumulative GC dose. Hip, spine and forearm BMDs were measured by duel-energy X-ray absorptiometry (DXA) at baseline and month 12. Patients were categorized into three groups according to pred use (never/<3/≥3 months) during the first year of follow-up. Patients who ever took>10mg/day of pred were excluded. The change in BMD was compared between groups and between the two time points.

Results: The baseline characteristics of patients were shown in Table 1. Patients

Table 1. Baseline characteristics

	Duration of pred use			
	Never (n=58)	<3 months (n=8)	≥3 months (n=41)	*p*
Female	46 (79.3%)	5 (62.5%)	28 (68.3%)	0.249
Age (years)	50.66±11.86	48.25±16.4	57.61±10.24	0.004
BMI (kg/m^2)	22.80±3.56	22.27±2.19	23.55±3.84	0.496
RF+ve	46 (79.3%)	6 (75.0%)	32 (80.0%)	0.950
AntiCCP+ve	41 (83.7%)	4 (80.0%)	31 (83.8%)	0.976
Osteoporosis	14 (24.1%)	2 (25.0%)	14 (34.1%)	0.540
Disease duration	10.80±11.41	7.49±3.99	6.73±6.11	0.032
Tender joints	6.77±5.19	6.25±4.17	9.85±7.92	0.218
Swollen joints	4.05±3.70	4.13±2.85	5.98±5.17	0.146
ESR (mm/1st hr)	56.93±35.62	40.75±18.97	62.20±35.72	0.387
CRP (mg/L)	15.18±21.68	14.8619.56	27.31±34.77	0.265
DAS-CRP	4.28±1.20	4.40±1.03	4.95±1.41	0.042
DAS remission	3 (5.3%)	0 (0.0%)	2 (4.9%)	0.436
Pred	0 (0.0%)	5 (62.5%)	25 (61.0%)	<0.001
Osteoporotic drug	0 (0.0%)	0 (0.0%)	2 (5.6%)	0.172
DMARDS	30 (54.5%)	4 (57.1%)	13 (36.1%)	0.332
Biologics	0 (0.00%)	0 (0.00%)	0 (0.00%)	–
NSAID	40 (72.7%)	5 (71.4%)	28 (77.8%)	0.766

who required ≥3 months of pred treatment are older, with a shorter disease duration and a higher disease activity. Significant differences in the percentage change of BMD in forearm was found among the groups (Pred never/Pred<3 months/Pred≥3 months: -2.99±4.21/-1.05±3.10/-0.65±3.45, p=0.045). Post-hoc analysis revealed that the percentage reduction of forearm BMD was significantly less in the Pred ≥3 months group compared to the Pred never group (p=0.043). After adjusting for age, gender, disease duration and baseline DAS-CRP, the changes in forearm BMD was still significantly different among the three groups (p=0.015). No significant differences in the changes of hip and spine BMD were observed. Significant changes in forearm BMD were observed between baseline and month 12 only in the Pred never group (0.54±0.08/0.53±0.0 p<0.001,graph1).



Conclusions: Small to medium dose of prednisolone might protect bone loss in forearm among early RA patients. These results need to be further validated.

References:

[1] Safety of low- to medium-dose glucocorticoid treatment in rheumatoid arthritis: myths and reality over the years. Ann N Y Acad Sci 2014.

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AB0222 THE SERUM ANTI-CITRULLINATED PROTEIN/PEPTIDE ANTIBODIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Objectives: To investigate the diagnostic value and prognostic usefulness of anti-citrullinated protein/peptide antibodies (ACPA) in children with juvenile idiopathic arthritis (JIA).

Methods: The presence of ACPAs in the serum samples from 81 JIA patients were determined using Anti-CCP IgG, CCCP3.1 IgG and IgA ELISA. Citrullinated Protein Antibodies, Anti-MCV, and Aeskulisa RA/CP-Detect which coated various citrullinated antigen substrates: synthetic cyclic peptide, recombinant rat filaggrin, mutated human vimentin, and IgG-derived peptides. 55 children with other joint diseases and 49 healthy donors were control groups. The diagnostic performance of ACPAs was analyzed and correlations between ACPAs and radiological damage were evaluated.

Results: CPAs in 8.8–28.4% of JIA group were detected with specificity of 84.6–98.1%. ACPAs could be seen in all subtypes of JIA, and high levels of ACPAs were particularly found in the RF positive JIA patients No healthy control had increased ACPA tested for CCP, CCP3.1, and CPA, whilst 3and 2 of healthy controls were found positive to MCV and RA/CP, respectively. The presence of ACPAs correlated more frequently with the presence of RF (P<0.05). The ACPA positivities in 18 JIA patients with radiological damage were 27.8–55.6%, which higher than that in patients without damage, and of the ACPA (CCP, CCP3.1, CPA, or MCV) positive JIA patients, 62.5%, 62.5%, 52.9%, 43.5% respectively had radiological damage, which significantly higher than that in JIA patients without ACPA (P<0.05).

Conclusions: This study confirms the main presence of ACPAs in children with polyarticular JIA, especially those with RF positive using ELISA based methods, and ACPAs relate significantly with joint erosions in JIA.

Disclosure of Interest: None declared

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AB0223 PROGNOSTIC FACTORS FOR RADIOGRAPHIC DAMAGE IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

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Background: Long since it have been suggested that seronegative rheumatoid arthritis (RA) represents a clinical entity quite distinct from that of seropositive RA. However, analytical studies dedicated to clinical outcomes regarding radiographic progression and risk factors for that are scarce[1,2].

Objectives: The aim of this study is to evaluate radiographic outcome and prognostic factors for radiographic damage in patients with seronegative RA.

Methods: RA pateints reportedly seronegative for both rheumatoid factor and anti-cyclic citrullinated peptide antibody who were seen at Jeju National University Hospital in South Korea between August 2003 and December 2016, and followed-up at least 2 years were included. Medical records, laboratory and radiographic data was retrospectively analyzed and multivariate analysis was performed to evaluate prognostic factors for radiographic damage in patients with seronegative RA.

Results: One hundred six patients with seronegative RA were observed and 16 (15.1%) patients demonstrated newly-developed joint damage during follow-up period. Age at diagnosis was 38.9 years and 64 (60.4%) patients were female. Symptom duration at diagnosis was 1.1 years and follow-up duration was 4.4 years. Baseline characteristics including sex, symptom duration, smoking status, number of active joints, acute phase reactant, joint erosion at diagnosis were not significantly different in patients with joint damage compared to those without joint damage. Joint erosion at diagnosis and smoking status were associated with radiographic damage in seronegative RA adjusting age, symptom duration, ESR, CRP values at diagnosis, and follow-up duration, whereas it was not statistically significant (adjusted odds ratio 1.45;p=0.061 and 1.58;p=0.072 respectively).

Conclusions: Our study demonstrated a rate of joint damage in patients with seronegative RA comparable to recent studies. Joint erosion at diagnosis and smoking status showed tendency to correlate with progression of radiographic damage in patients with seronegative RA. A large comparative study dedicated to this issue in seronegative RA is required.

References:

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AB0224 SIMULATION FOR CHOICE OF BDMARDS AND TSDMARDS IN ORDER TO SUCCESS FOR THREE-YEAR SURVIVAL IN RHEUMATOID ARTHRITIS TREATMENT

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Background: In rheumatoid arthritis (RA) treatment, bDMARDs and tsDMARDs (BIO) perform tremendous disease activity control, however, its effectiveness is uncertain and unstable, because their survival ratio is not good enough to tolerate. If more right choice is done in guided by some simulation.

Objectives: This study aims more than 80% of three-year survival ratio (SR@3Y) in simulating risk of BIO by using statistical clinical data and post marketing surveillance (PMS) data with Bayes estimation.

Methods: Infection risk and survival risk were harvested from Japanese PMS data, and our clinical data. All our cases were calculated with last observation carried forward method (LOCF). If BIO was continued for more than three years or discontinued by attaining clinical remission, it was evaluated as success, while other cases were evaluated as failure. Patient's clinical data and general status were calculated for each case, and SR@3Y for success was statistically evaluated with Binary Logistic Analysis for success. Evaluation methods for parameters were divided according to general risk and drug specific possibility. If calculated general risk went above 0.2, selection of BIO was discarded. In other case which had gone below, choice of BIO is done in according to point that had been cumulated by drug specific possibility in choosing what took maximum calculated expectation value.

If chosen drug have matched used BIO, it was evaluated as true, if not, it was evaluated as false, while if true case was in success, it was evaluated as true success, and if in failure, it was evaluated as true failure, while false case was in success, it was evaluated as false success, and if in failure, it was evaluated as true failure. Sensitivity in success cases and specificity in failure cases was evaluated in patients in whom BIO was administered. Statistical evaluation was done with chi-square test.

Results: 188 cases have had enough data for simulating. In these, 108 were success and 80 were failure. In success cases, simulated TNF inhibitor (TNF-i) counted 73, Tocilizumab (TCZ) counted 11, Abatacept (ABT) counted 12, and