treatments was positively associated with DAS28 remission (OR 1.11 per year increase, 95% C.I. 1.03–1.18, p=0.003).
Conclusions: The duration of biologic treatment and the number of previous biologic switches were not associated with of DAS28 remission. Indeed, a longer survival of biologic treatments was associated with remission. The mean survival of biologic treatments reflects both a smaller number of biologic failures and a prolonged response to each biologic treatment.
Disclosure of Interest: None declared
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AB0216 EFFECTS OF ANTI-CITRULLINATED PROTEIN ANTIBODIES ON SYSTEMIC BONE MASS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Bone loss in rheumatoid arthritis (RA) is a key feature both local and systemic. Anti-citrullinated protein antibodies (ACPA) have recently been found to directly induce differentiation and activation of osteoclasts and therefore contribute to periarticular bone loss.
Objectives: The aim of this study was to analyze the effect of ACPA on systemic bone mineral density (BMD) in patients with established RA.
Methods: This is a cross-sectional study with a single-center RA population. BMD was measured with Dual X-ray absorptiometry at lumbar and femoral sites. ACPA were measured by EIA. Multivariate analysis was performed adjusting for the main confounding variables.
Results: One hundred twenty-seven RA patients were enrolled. In univariate analysis ACPA-positive patients showed lower BMD Z-score (SD below the age- and gendermatched mean reference value) at femoral sites ($p<0.01$). A negative correlation between ACPA titer and BMD Z-score at all sites was observed ($p<0.01$). The multivariate analysis adjusted for the main confounding variables confirmed the negative effect of ACPA at femoral sites ($p<0.05$), but not at lumbar spine BMD. No significant effect of rheumatoid factor has been observed.
Conclusions: ACPA have a negative titer-dependent effect on BMD at femoral sites, mainly constituted by cortical bone. ACPA-positive patients, especially if at high titer, should undergo bone investigations and be treated with bone protecting agents. Disease-modifying anti-rheumatic drugs lowering ACPA titer might have positive effects on systemic bone mass.
Disclosure of Interest: None declared
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AB0217 THE PROGNOSTIC VALUE OF IGA AUTOANTIBODIES (RHEUMATOID FACTOR AND ACPA) FOR PREDICTION OF THERAPEUTIC RESPONSES TO ANTI-TNF THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) are important diagnostic markers in rheumatoid arthritis (RA). These antibodies are predominantly of the IgM (RF) or IgG (ACPA) isotype. The added diagnostic and prognostic value of IgA autoantibodies is being debated.
Objectives: To determine the prevalence of IgA-RF and IgA-ACPA in patients with RA and to investigate their potential predictive value regarding response to treatment with methotrexate (MTX) and TNF inhibitors.
Methods: A total of 255 patients were tested for the presence of IgA-RF, IgA-ACPA and IgG-ACPA by EliA® (Thermo Fisher Scientific); IgM-RF was measured by nephelometry. Therapeutic responses to MTX and TNF blocking biologicals were calculated in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses simplified disease activity index (SDAI) 50 and American College of Rheumatology (ACR) 20 responses were calculated.
Results: Among the 255 patients tested 125 (49%) had at least one type of IgA autoantibody: 114 (44.7%) were found to be IgA-RF positive and of these 10.5% were negative for IgM-RF and 5.2% were double negative for both IgM-RF and IgG-ACPA; thus, in these patients IgA-RF was the only detectable antibody. IgA-ACPA were detected in 79 (31%) patients and apart from one exception all of them had also IgG-ACPA. Remarkably, the percentage of patients showing a SDAI50 response to TNF inhibitors was significantly lower in patients positive for IgA-RF and/or IgA-ACPA ($p<0.0001$) compared to IgA negative patients. Thus, 58% of IgA negative (but IgM-RF and/or IgG ACPA positive) patients showed a SDAI50 response whereas only 25% of the IgA-RF and/or IgA-ACPA positive ones were responders. Interestingly, while the presence of both IgA specificities did not further change the percentage of responders, patients positive for IgA-ACPA but negative for IgA-RF showed the lowest response rate to anti-TNF treatment. Completely seronegative patients also showed a significantly lower SDAI50 response ($p<0.0001$) to TNF inhibitors compared with the IgA negative (but IgM-RF and/or IgG-ACPA positive) patients. Similar results were obtained when ACR20 was used as response criteria. No differences between the various serological groups were seen with respect to treatment with MTX.
Conclusions: While the added diagnostic value of IgA antibody measurement was moderate, IgA-RF and particularly IgA-ACPA appear to be associated with poorer therapeutic responses to TNF inhibitory biological drugs and therefore may help in further stratification of RA patients and therapeutic decision making.
Disclosure of Interest: None declared
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AB0218 CORRELATION OF GRAY SCALE AND POWER DOPPLER ULTRASONOGRAPHY WITH CLINICAL EVALUATION IN RHEUMATOID ARTHRITIS

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Objectives: Ultrasonography (US) is a useful method for assessing synovial vascularization and proliferation in rheumatoid arthritis (RA). The aim of the study is to compare the tender joint and swollen joint in patients with rheumatoid arthritis (RA) with gray scale (GS) and power doppler (PD) ultrasonography (US).
Methods: Thirty RA patients were included. Median disease duration was 53.7 months. Demographic and clinical data, C reactive protein (CRP) level and erythrocyte sedimentation rate (ESR) were recorded for each patient. Disease activity was evaluated using the Disease Activity Score in 28-joints (DAS28) with a median score 3.8.The joint tenderness and swelling were assessed for 10 joints (wrists, second and third proximal interphalangeal and metacarpophalangeal) in each patient.These joints were evaluated by GS and PD by ultrasonography. US joint effusion, synovitis and PD signals were graded from 1 to 3 for each joints. The 10-joint GS and 10-joint PD scores were then calculated. Correlations were tested using the Spearman coefficient.
Results: GS effusion, synovitis scores ($r=0.565$, $p<0.001$) and PD signals ($r=0.883$, $p<0.001$) correlated highly with the corresponding swollen joints. There was a significant correlation between DAS28 and number of tender joints ($r=0.745$, $p<0.001$) but no correlation was found between the tender joints and ultrasonographycal effusion, synovitis grade ($r=0.073$, $p>0.001$) and the PD signal ($r=0.069$, $p>0.001$). There was moderate correlation between 10 joints GS, 10 joints PD and DAS28, but it was not statistically significant.

Table 1. Demographic and clinical characteristics of the patients (n=30)

Age (years) – mean (SD)	53.7±11.9
Female, n (%)	28 (93.3)
RA duration (months)	42 (67)
Rheumatoid factor positive, n (%)	15 (50)
CCP positive, n (%)	20 (66.7)
Smoking, n (%)	5 (16)
Prednisone, n (%)	11 (36.7)
DAS28 (ESR), (IQR)	3.8 (2.9)
TJC (0–10), (IQR)	2 (5)
SJC (0–10), (IQR)	0 (0)
10 Joint GS score, (IQR)	0 (1)
10 Joint PD score, (IQR)	0 (0)
ESH mm/h (IQR)	23.5 (21)
CRP mg/L (IQR)	4.6 (6.5)

SD: standard deviation, RA: rheumatoid arthritis, CCP: cyclic citrullinated peptide, DAS28: disease activity score in 28 joints, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, GS: gray scale, PD: power doppler, TJC: tender joint count, SJC: swollen joint count.

Conclusions: Evaluating the swollen joints with clinical examination and combining it with US is a sensitive method. As joint tenderness is a more subjective finding than the joint swelling, this may explain the lack of correlation between tender joints and ultrasonography findings. We suggest to use Gray scale US and PD as a complementary method in addition to clinical assessment of joint tenderness in patients with RA.
Disclosure of Interest: None declared
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AB0219 INTENSIVE COMBINATION THERAPY WITH MEDICATION AND ORTHOPEDIC SURGICAL INTERVENTION FOR TREATING RHEUMATOID ARTHRITIS PATIENTS WITH DETERIORATED JOINTS

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Background: The treatment aim of rheumatoid arthritis (RA) is achieving and maintaining remission (REM) or low disease activity (LDA) via tight medical control. However, despite remarkable advances in medication, progressive deterioration and/or deformity of the joint sometimes occurs, if adequate medication is not administered in the early stage. Surgical reconstruction is still required in the joints with functional loss caused by structural damage. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and improved mental wellness.
Objectives: The objective of this study was to clarify the effectiveness of intensive combination therapy with medication and orthopedic surgical intervention in patients who have already achieved REM or LDA.

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.

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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.

Disclosure of Interest: None declared
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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