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THU0059 **INCIDENCE OF JOINT REPLACEMENT SURGERY AMONG BIOLOGICS AND NON-BIOLOGICS TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: A PROPENSITY SCORE MATCHED COHORT STUDY FROM DENMARK**

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Background: Biologics have improved several clinical, patient-reported and radiological outcomes in patients with rheumatoid arthritis (RA), but little is known about the potential impact on the need for joint replacement surgery.

Objectives: To investigate the incidence of joint replacement surgery among biologics treated compared with biologics naïve patients with RA.

Methods: A nationwide, register-based propensity score matched cohort study. RA patients registered between 2006 and 2016 in the DANBIO register with a disease duration ≤ 2 years were identified. Patients initiating their first treatment series with biologics were followed up to 10 years for a first joint replacement of the hip, knee, shoulder, elbow and finger/wrist. Biologics naïve patients were followed up for the same outcome from their first clinical visit registered in DANBIO. Following a 1:n propensity score matching, Cox-models were undertaken to calculate the hazard ratio (HR) for a first joint replacement surgery among biologics compared with non-biologics treated RA patients. Further, subgroup analyses based on within-strata propensity score matched patients were carried out. All information on surgical outcomes was obtained in the Danish National Patient Registry.

Results: In total, 1187 biologics treated were matched with 3666 non-biologics treated patients (See Table).

Abstract THU0059 – Table1. Baseline characteristics of biologics treated and biologics naïve patients with rheumatoid arthritis and a disease duration < 2 years registered in DANBIO between 2006 and 2016.

	Biologics treated	Biologics naïve	SMD
N Total	1187	3666	
Female, n (%)	828 (70)	2546 (69)	0.01
Age at start of follow-up, mean (s.d)	53.8 (13.5)	54.1 (15.1)	0.02
Age at diagnosis, mean (s.d)	52.7 (13.5)	52.9 (15.1)	0.02
IgM-RF and/or ACPA positive at start of follow-up, n (%)	686 (58)	2042 (56)	0.04
DAS28-CRP	4.5 [3.6 to 5.4]	4.5 [3.4 to 5.4]	0.03
HAQ-DI	1.00 [0.50 to 1.62]	1.00 [0.50 to 1.62]	0.03
CRP mg/ml	9 [3 to 22]	9 [3 to 20]	0.02
VAS physician global	32 [18 to 49]	30 [16 to 50]	0.04
VAS pain	53 [31 to 73]	52 [30 to 74]	0.01
Methotrexate, n (%)	1044 (88)	3160 (86)	0.06
Glucocorticoid, n (%)	246 (21)	718 (20)	0.04
Chronic obstructive pulmonary disease, n (%)	168 (5)	57 (5)	0.01
Cardiovascular disease, n (%)	322 (9)	97 (8)	0.02
Hospitalised with infection in previous 5 years, n (%)	128 (4)	43 (4)	0.01

Abbreviations: SMD, absolute standardized mean difference; s.d., standard deviation; VAS, visual analogue scale. All values are median [interquartile range] unless otherwise stated. During follow-up, 43 biologics-treated and 124 naïve patients had a first joint replacement surgery corresponding to an overall HR of 0.95 (0.65 to 1.40) for biologics treated compared with naïve patients (Figure 1). Patients with a DAS28-CRP < 4.6 at start of follow-up (low and moderate disease activity)¹, biologics treated had a lower risk of joint replacements compared with biologics naïve patients.

Conclusion: In this nationwide Danish cohort study, there was no difference in the incidence of joint replacement surgery among newly diagnosed RA patients selected for treatment with biologics compared with patients naïve to biologics.

Figure 1. Overall and sub-group hazard ratios for a first joint replacement surgery among newly-diagnosed patients with rheumatoid arthritis and treated with biologics compared with propensity score matched patients naïve to biologics.

Abstract THU0059 – Figure 1

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THU0060 **ELEVATED SYNOVIAL MUC1 EXPRESSION IS ASSOCIATED WITH JOINT DAMAGE AND ONE-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS**

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Background: The tumor-like transformation of synovium, especially the lining layer, play a critical role in joint damage in rheumatoid arthritis (RA) by forming aggressive and invasive rheumatoid pannus, but the underlying mechanisms remains unknown. Mucin1(MUC1), an O-glycosylated protein participating in forming protective mucous barriers on epithelial surfaces and intracellular signaling, has been found aberrantly expressed in many cancers and implicated in tumor progression and metastasis. However, the expression of MUC1 in synovium and its role in RA is unclear.

Objectives: We aimed to investigate the expression of MUC1 in RA synovium and its correlation with joint destruction in RA patients.

Methods: Synovial tissue (ST) were sampled by Parker-Pearson needle biopsy from 67 RA patients who had completed one year follow-up from a prospective RA cohort [1]. ST from 13 patients with orthopedic arthropathies (Orth. A) with arthroplasty or arthroscopy were used as control. Expression of MUC1 in ST was assessed by immunohistochemistry (IHC). Radiographic assessments of hand/wrist at baseline and month 12 were performed with the Sharp/van der Heijde-modified sharp score. Radiographic joint damage (RJD) was defined as total modified Sharp score (mTSS) >10. Radiographic progression (RP) was defined as a change of mTSS more than 0.5 units.

Results: 1. Both nuclear and cytoplasmic MUC1 expression were observed in lining and sublining cells of synovium. The percentage of MUC1+ lining cells was significantly higher in RA (median 65.4%, IQR 53.6% 73.2%) than that in Orth. A (median 43.1%, IQR 3.4% 68.4%, $P < 0.05$).

2. Thirty-five (52%) RA patients showed RJD at baseline and their MUC1 expression in lining layer was significantly enhanced compared with RA patients without RJD (median 69.6%, IQR 64.5% 76.8% vs. median 58.9%, IQR 39.8% 67.9%, $P < 0.01$). Spearman's rank order correlation test showed significantly positive correlations between the percentage of MUC1+ lining cells with mTSS, joint space narrowing (JSN) subscore and joint erosion (JE) subscore at baseline ($r = 0.303-0.426$, all $P < 0.05$).

3. Furthermore, twenty-two (33%) patients suffered from one-year RP and they showed significantly positive percentage of MUC1+ lining cells than non-progressive patients (median 71.2%, IQR 55.2% 75.2% vs. median 64.1%, IQR 55.2% 75.2%, $r < 0.01$). The percentage of MUC1+ lining cells was positively correlated with mTSS, JSN and JE subscores at month 12 ($r = 0.310-0.405$, all $P < 0.05$). ROC curve analysis showed that the tradeoff value of MUC1+ lining cells for predicting one-year RP was 69% with sensitivity 72% and specificity 71% (AUC=0.661, 95% CI=0.516 0.805, $P=0.034$). Univariate logistic regression analysis showed that high MUC1+ lining cells was a significant predictor of one-year radiographic progression (OR: 5.893, 95%CI: 1.934 17.956, $P=0.002$).

Conclusion: Our data showed elevated MUC1 expression in RA synovial lining cells was positively correlated with joint damage and predicted one-year radiographic progression, which imply that MUC1 might be involved in the pathogenesis of RA joint destruction.

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THU0061

IN OVERWEIGHT SUBJECTS, SERUM ADIPONECTIN PREDICTS THE DEVELOPMENT OF RHEUMATOID ARTHRITIS INDEPENDENTLY OF OTHER ADIPOKINES

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Background: Adipokines, such as adiponectin, leptin, resistin and visfatin, are cytokines produced by the adipose tissue and involved in metabolism and inflammation¹. Adiponectin is elevated in both serum and synovial fluid of subjects with rheumatoid arthritis (RA), suggesting a possible role of this adipokine in the pathogenesis of RA^{2,3}. Circulating levels of leptin, resistin, and visfatin are also higher in subjects with RA compared to controls^{2,4}.

Objectives: Aim of this study was to determine if adiponectin, leptin, resistin, and visfatin predict the development of RA.

Methods: Two nested-case control studies were performed including pre-symptomatic participants of two cohorts from Sweden: the Swedish Obese Subjects (SOS) study and a cohort of individuals identified within the Medical Biobank of northern Sweden. The SOS is a clinical trial including 4047 subjects with obesity⁶. During a follow-up for up to 29 years, 92 subjects developed RA. Among those 92 subjects, 82 subjects with available serum at baseline were matched 1:5 with 410 subjects who did not develop RA during follow-up. Matching was based on baseline age, sex,

body-mass index (BMI), bariatric surgery yes/no, year of inclusion, and smoking. A nested case-control study of 88 sex- and age-matched pairs was performed within the Medical Biobank of Northern Sweden using blood samples donated before the onset of the first RA symptoms. The pre-dating time before onset of symptoms of RA was 8.5 ± 5.0 years⁷.

Baseline serum levels of adiponectin, leptin, resistin, and visfatin were measured using the Quantikine ELISA kit from R&D Systems (Wiesbaden, Germany). Visfatin could not be measured in the Biobank cohort, due to lack of serum. Both binary logistic as well as conditional logistic regression analyses were used to determine if adipokines were elevated years before the onset of RA.

Results: In a multivariable analysis including adiponectin, leptin, resistin, visfatin performed in the SOS cohort, serum adiponectin was associated with a higher risk for RA independently of other adipokines (Odds ratio, OR, 1.1, 95% confidence interval, CI, 1.0-1.1, p value=0.01). Leptin, resistin and visfatin levels were not associated with the risk of RA.

In the Biobank cohort, no association between adipokines and risk for RA was detected. However, when stratifying the population according to BMI, in the subgroup having BMI>25 ($n=109$), adiponectin levels were associated with higher risk for RA (OR 1.2, 95% CI 1.0-1.36, $p=0.03$), independently of leptin and resistin levels. Virtually the same results were obtained in both the SOS and the Biobank cohorts when conditional logistic regression analysis was used.

Conclusion: Our results suggest that higher serum adiponectin levels predict the development of RA in subjects with overweight/obesity.

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THU0062

THE DYSREGULATION OF NK CELLS AND NON-CLASSICAL AND CLASSICAL MONOCYTE SUBPOPULATIONS IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Antibodies against citrullinated proteins (ACPA) are present months to years before the clinical manifestation of rheumatoid arthritis (RA). ACPA+ individuals are at 8-10x higher risk of developing RA compared to seronegative individuals. EULAR characterised individuals with arthralgia suspicious for progression to RA based on their clinical features (clinically suspect arthralgia, CSA).

Objectives: The alteration of natural killer (NK) cells and monocyte subpopulations in patients with established RA has been previously described. We therefore aimed to study the lymphocyte and monocyte subpopulations in individuals in the preclinical phase of RA.

Methods: Our study included 49 individuals with arthralgia (mean age 45.97 ± 11.95 years; 92% females) and 80 age and gender matched healthy controls (HC). Leukocytes from peripheral blood were analysed by flow cytometry. Lymphocyte subpopulations were defined as B (CD19