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FRI0155 PREVALENCE OF HBV INFECTION AND RISK OF REACTIVATION ON BIOLOGIC TREATMENT: A POPULATION-BASED OBSERVATIONAL STUDY OF RHEUMATOID ARTHRITIS SUBJECTS IN A NORTHERN ITALY AREA

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Background: The introduction of biologic agent's treatment in rheumatic diseases dramatically changed their outcome, but raised some concerns about infections recrudescence. Due to the prevalence of hepatitis B virus (HBV) among Italian general population (2–6%), the possibility of a disease reactivation in case of an immunosuppressive treatment has to be considered.

Objectives: Aim of this prospective, population-based observational study was to assess the prevalence of HBV (both in chronic carriers and reactivated) rheumatoid arthritis (RA) patients in our setting; to verify if these findings were in line to the Italian and European-reported data; finally, to evaluate the final outcome of HBV RA subjects.

Methods: We enrolled the totality of RA patients treated by biologics and, therefore, consulting our Unit at least every 12 weeks, from December 2015 to January 2017. According to the current (ACR/EULAR and AASLD) guidelines, every subject was screened for HBV before starting biologic treatment. Descriptive statistics was performed. Acute infection; previous (resolved) infection; inactive and active carrier; and vaccine-immunized subjects were defined according to Tab. I.

Results: A totality of 265 RA patients (female 56.3%; male 43.7%; mean age 36±20 years) underwent biologic treatment after succeeding the screening (HBsAg+ subjects were excluded). The huge majority of them (82%) was treated by TNF-alpha inhibitors (TNFi), since the remaining received biologic agents with different mechanisms of action. We overall detected 33 (12.5%) inactive carriers, for whom HBsAg and HBV DNA periodical monitoring was suggested; in 3 of them (1.1% of the study population), HBV DNA became detectable, with a low viral load (<2000 IU/ml): they prosecute the biologic therapy after the introduction of the standard prophylaxis (lamivudine 100 mg daily) and a more strictly (periodic liver enzymes and liver ETG evaluation) monitoring. In occasion of the screening, we observed 6 (2.3%) HBV-immunized (due to vaccine) and 6 (2.3%) previously infected (HBcAb+) patients: for the first ones no action is required, since the latter were put on standard prophylaxis before undergoing biologic agent and monitored. One of them (0.38%) developed, after 6 months of treatment, HBV reactivation with high-level (>2000 IU/ml) detectable DNA and liver enzymes elevation (>normality x3). She was therefore stopped from receiving biologic agent and put on entecavir 1 mg daily.

Interpretation of HBV serologic test results

	HBsAg	HBsAb	HBcAb	HBcAb	HBcAg	HBV DNA
Acute infection	POS	neg	POS	neg	POS	POS
Past infection (resolved)	neg	POS	neg	POS	neg	neg
Inactive carrier	POS	neg	neg	POS/neg	neg	neg
Active carrier	POS	neg	POS	POS	POS/neg	POS
Vaccine induced immunity	neg	POS	neg	neg	neg	neg

POS: positive; neg: negative; HBsAg: hepatitis B surface antigen; HBsAb: hepatitis B surface antibody; HBcAb: hepatitis B core antibody; HBcAg: hepatitis B envelope antigen.

Conclusions: Our prospective, population-based observational study, performed in a first-level referring Hospital in a highly populated area, suggests some considerations. In a way, our data reported a significantly higher prevalence of HBV infection "contact" among our RA population, in comparison to the general one (p<0.05). This issue has previously been reported and could be justified but the generally higher HBV diffusion in certain area (i.e., Italy); by the age/ethnicity of the sample; and, finally, by the bias consisting in an extensive screening of these patients. On the other hand, our experience suggests that a tight monitoring of parameters predicting infectious flare should lead to a prompt diagnosis and a lower number of complications for these peculiar patients, as observed in our population.

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FRI0156 DO CHANGES IN ADIPOCYTOKINES CORRELATE WITH CHANGES TO DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS? FINDINGS FROM THE TOMORROW STUDY

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Background: Cytokines released from mast cells evoke inflammation and correlate with arteriosclerotic lesions and autoimmune disease¹. The relationship between disease activity and lipid metabolism is a notable in research surrounding rheumatoid arthritis (RA). RA patients without disease control reportedly show high titers of leptin or adiponectin as adipocytokines².

Objectives: We analyzed the interaction between changes in disease activity and adipocytokines using data from the TOMORROW (Total Management Of Risk factors in Rheumatoid arthritis patients to Lower morbidity and mortality clinical trial) study, a 10-year prospective study (registration number, UMIN00003876).

Methods: We analyzed data collected from the cohort of the TOMORROW study including 193 patients with RA and age- and sex-matched 194 healthy individuals (controls). We compared changes in leptin and adiponectin (Δ leptin and Δ adiponectin) in both groups between baseline and after 3 years. Correlations with the change in disease activity (Δ DAS28ESR) during 3 years and changes in Δ leptin and Δ adiponectin in RA were investigated by univariate analysis.

Results: Leptin levels increased in both groups. No significant differences in Δ leptin were seen between RA (0.21 ng/ml) and controls (0.18 ng/ml; p=0.37). On the other hand, adiponectin was significantly decreased in controls (-3.3 μ g/ml) compared to RA (-1.8 μ g/ml; p=0.01). Negative correlations between Δ leptin and Δ adiponectin were detected in the RA group (r=-0.29, p<0.01). The correlation between adiponectin and DAS28ESR was positive both at baseline (r=0.22, p=0.01) and after 3 years (r=0.18, p=0.01). However, no such tendencies were seen for leptin. Table 1 shows details of the correlations with changes in adipocytokine. In terms of the relationship with Δ DAS28ESR, no correlation was seen with Δ leptin (r=0.07, p=0.31) or Δ adiponectin (r=-0.01, p=0.91). Changes in lipid metabolic markers and fat percentages were detected as predictive factors for Δ adipocytokines.

Table 1. Correlations with changes in adipocytokine by univariate analysis

	R	P
Δ Adiponectin		
Baseline age	-0.199	0.006
Δ High-density lipoprotein	0.265	0.001
Δ Fat percentage	-0.144	0.046
Δ DAS28ESR	-0.009	0.906
Δ Leptin		
Baseline age	0.258	0.001
Δ Low-density lipoprotein	0.347	0.001
Δ fat percentage	0.554	0.001
Fall	-0.145	0.045
Δ DAS28ESR	0.074	0.311

Conclusions: Leptin increased and adiponectin decreased over the course of 3 years. Correlations between Δ adipocytokines and Δ DAS28ESR were not detected. RA patients with high disease activity show higher adiponectin titers.

References:

- [1] Benoist C., Mathis D. Mast cell in autoimmune disease. *Nature*. 2002; 420: 875–8.
- [2] Cho H., Lin J., Chen W., et al. Baseline adiponectin and leptin levels in predicting an increased risk of disease activity in rheumatoid arthritis: a meta-analysis and systematic review. *Autoimmunity*. 2016; 49: 547–53.

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FRI0157 FERTILITY IN WOMEN WITH RHEUMATOID ARTHRITIS COMPARED TO HEALTHY CONTROLS

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Background: Data suggest infertility is increased in women with rheumatoid arthritis (RA) compared to healthy women. Therefore, it is possible that diminished ovarian reserve and ovulatory dysfunction may be more common among women with RA.

Objectives: To compare differences in ovarian reserve and ovulatory frequency, as well as in self-reported infertility, between women with and without RA.

Methods: Women with RA aged 20–40 seen in a university clinic without a history of ovarian surgery or prior exposure to possible ovary-toxic medications were invited to participate in a cross-sectional survey. Healthy controls were women aged 20–40 without an autoimmune disease, matched for age and current use of hormonal contraceptives. Infertility was defined as a patient reporting physician-diagnosed infertility or being unable to get pregnant after 12 months of trying. Ovarian reserve was assessed by measuring anti-Müllerian hormone (AMH). In women who were not taking hormonal contraceptives, progesterone level was measured from a serum sample drawn between days 21 and 23 of the menstrual cycle. Anovulation was defined as a progesterone level <3 ng/mL. In

descriptive comparisons, differences in proportions were determined by Fisher's exact test, and ANOVA determined differences in means for continuous variables. Multivariate linear models estimated the effect of RA on AMH. In women with RA, the effect of RA medication use on AMH and anovulation was explored.

Results: There were 75 RA patients (83% Caucasian, 4% Hispanic, 77% with at least a college education) and 75 controls (64% Caucasian, 5% Hispanic, 88% with at least a college education). The majority of RA patients were married (60%), compared to 31% of controls. The mean age of both RA patients and controls was 32 years. Mean AMH in RA patients was 3.0 (SD: 2.6) compared to 3.9 (SD: 3.9) in controls (p-value: 0.1). In linear regression models adjusted for age, hormonal contraceptives and race (nonwhite vs. white), RA patients had a lower AMH than healthy controls (β : -1.05; 95% CI: -2.09, -0.005; $p=0.05$). There was no observed difference in the proportion of RA patients and controls with anovulation (19% in RA and 21% in controls). Infertility was reported by 12% of RA patients and 7% of controls ($p=0.4$).

Among RA patients, 81% reported having ever used methotrexate (MTX). The mean AMH for MTX users was 2.8 (SD: 2.4) compared to 4.0 (SD: 3.1) in never users ($p=0.1$). In linear regression models adjusted for age, hormonal contraceptives and race, RA patients who had ever taken MTX had a lower AMH than those who had never taken MTX (β : -1.49; 95% CI: -2.83, -0.15; $p=0.03$). However, when the cumulative dose of MTX was analyzed, there was no effect of cumulative MTX and AMH. Ever use of prednisone or NSAIDs did not appear to affect AMH levels in RA patients. Methotrexate, prednisone, and NSAIDs use did not have an observed effect on anovulation.

Conclusions: In this cross-sectional study, women with RA appeared to have a lower AMH level than healthy controls, suggesting ovarian reserve may be lower in these patients. In RA patients, previous use of methotrexate was associated with lower AMH, although no dose response of cumulative methotrexate exposure was observed. We did not observe a difference in anovulation between RA patients and controls. This suggests women with RA may have reduced fertility for reasons other than anovulation.

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FRI0158 CAROTID ENLARGEMENT, BRACHIAL ARTERY FLOW-MEDIATED VASODILATATION AND SERUM LEVELS OF VON WILLEBRAND FACTOR IN RHEUMATOID ARTHRITIS

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Background:

In rheumatoid arthritis (RA), higher mortality is mainly due to cardiovascular disease, as a consequence of accelerated atherosclerosis found in this diseases (1). Finding methods for assessing vascular dysfunction during the early stages of the disease is important, particularly in patient groups at high CV risk (2).

The use of noninvasive imaging techniques may help identify high-risk individuals who may benefit from active therapy to prevent clinical disease. Two of them, brachial ultrasonography to determine the presence of endothelial dysfunction and carotid ultrasonography to assess carotid intima-media wall thickness (IMT) have been found to be useful in the assessment of the cardiovascular risk of patients with RA (3). Prothrombotic markers have been shown to be able to predict cardiovascular risk in patients with RA (4).

Objectives: The first aim of the study was to investigate whether early signs of atherosclerosis and endothelial dysfunction, as measured by IMT and brachial artery flow-mediated (FMD) vasodilatation, were present in patients with RA compared with controls. The second aim was to analyze correlation between serum levels of vWF and IMT and FMD in patients with RA.

Methods: Fifty-two patients with RA and 30 matched healthy controls without clinically evident CV disease were studied. Brachial and carotid ultrasonography was performed to determine FMD and IMT, respectively. We also assayed immunological, inflammatory and metabolic laboratory markers.

Results: IMT was significantly higher in RA patients (1.00 ± 0.16 mm) patients than in controls (0.89 ± 0.13 mm) ($P=0.001$). FMD% was significantly lower in RA (9.16 ± 7.03) as compared to controls (12.60 ± 5.49) ($p=0.005$). It showed statistically higher values of vWF in the RA patients compared to the control group ($p=0.01$).

Patients with RA is divided into two groups according to the value of the IMT, below 9mm and 0.9mm and above. vWFAct is statistically significantly higher in the group with thicker IMT ($p=0.046$), as well as the percentage of men ($p=0.030$). Other parameters did not show statistical significance in relation to the value of the IMT.

Conclusions: In patients with RA, increased serum levels of vWF and impaired FMD and IMT, indicating endothelial dysfunction and accelerated atherosclerosis. IMT measurement is the first candidate to evaluate against conventional evaluation of cardiovascular risk in prospective studies.

References:

- [1] Dessein PH, Joffe BI, Singh S. Biomarkers of endothelial dysfunction, cardiovascular risk factors and atherosclerosis in rheumatoid arthritis. *Arthritis Res Ther* 2005;7:634-643.
- [2] Tousoulis D, Antoniadou C, Bosinakou E et al. Differences in inflammatory and

thrombotic markers between unstable angina and acute myocardial infarction. *Int J Cardiol* 2007;115:203-207.

- [3] Fuchs I, Frossard M, Spiel A, Riedmuller E, Laggner AN, Jilma B. Platelet function in patients with acute coronary syndrome (ACS) predicts recurrent ACS. *J Thromb Haemost* 2006;4:2547-2552.

- [4] Jonsson SW, Backman C, Johnson O et al. Increased prevalence of atherosclerosis in patients with medium term rheumatoid arthritis. *J Rheumatol* 2001;28:2597-2602.

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FRI0159 INFECTION AND MALIGNANCY ARE NOW THE MAJOR CAUSES OF DEATH IN AGGRESSIVELY TREATED RHEUMATOID ARTHRITIS PATIENTS

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Background: Patients with rheumatoid arthritis (RA) have an increased mortality compared to the general population. Previous studies have shown that this is attributable to cardiovascular and respiratory disease. Over recent years earlier and more aggressive treatment with higher dosage of methotrexate and the earlier use of biologic drugs has improved disease outcomes. The effect on cause of death is unknown. In this retrospective cohort study we found the major cause of death was infection followed by malignancy and found no correlation with seropositivity or gender.

Objectives: To analyse the causes of death in RA patients treated with aggressive disease modifying anti rheumatic drugs (DMARD) and Biologic therapies in Berkshire, UK.

Methods: Patients with RA who died between 2010 and 2016 were identified using the DAWN software DMARD monitoring database. A cohort of 3106 patients with RA are monitored using DAWN software in Berkshire, UK. The causes of death were identified from medical records, general practice records or the local coroners office.

Results: 198 patients on DAWN monitoring died during the 6 year study period. Treatment details and cause of death was identified for 131 RA patients. 71% were seropositive for rheumatoid factor and 61% were female.

91 patients (69%) were treated with methotrexate, 28 hydroxychloroquine (21%), 14 sulphasalazine (21%) and 7 with leflunomide (5%). The majority of patients (81) were on monotherapy (61%), 32 were on 2 DMARDS (24%) and only one was on triple therapy.

4 patients with RA who died were on biologic monotherapy, 10 were treated with biologic and combination DMARD. The most commonly prescribed biologics were etanercept (35%) and rituximab (35%).

The leading causes of death in this cohort were pneumonia (39 patients 29%), cerebrovascular disease (16 patients 12%), septicemia (11 patients 8%) and lung cancer (6 patients 4%).

Infection accounted for 57 patients' deaths (43%) followed by malignancy in 24 patients (18%). Cerebrovascular disease (20 patients, 15%) and cardiovascular disease (13 patients, 9%) were less frequent causes of death in our cohort.

Comorbidity data for the cohort was recorded pre-mortem. 49 patients (37%) had cardiovascular disease of any kind. 25% had respiratory disease and 23% had an endocrine comorbidity (predominantly diabetes).

Conclusions: In our large cohort of aggressively treated RA patients, infection followed by malignancy and not cardiovascular disease, was the leading cause of death. Larger prospective studies will be required to see if cumulative drug toxicity of more aggressive early treatment improves outcome from RA but changes mortality from comorbidities over time.

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FRI0160 EVALUATION OF INFLAMMATORY CARDIOVASCULAR (CV) RISK FACTORS IN PRE- AND POST-MENOPAUSAL FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Objectives: To assess inflammatory factors and peripheral vessels involvement as markers of cardiovascular risk in female patients with RA

Methods: 105 female patients who fulfill ACR/EULAR 2010 criteria were examined. Laboratory assessments consisted of biochemistry and hematology analysis, measuring of CRP level, rheumatoid factor, anti-CCP level, total cholesterol, HDL, LDL, thyroglobulin, apolipoprotein, A1, apolipoprotein B, uric acid, HbA1c, microalbuminuria. DAS28 was used in characterizing RA activity. CV risk was defined per mSCORE. Tibial artery and carotid artery ultrasonography examination included the measurement of cIMT in 3 points, detection of focal plaques in the extracranial carotid tree, blood flow velocity and morphology of the intima was performed

Results: 83.3% reproductive age patients were without CV risk, 11.1% experienced middle level and 5.6% low level of CV risk on mSCOR. In 96.1% postmenopausal patients moderate, high and very high CV risk was detected. According to multiple logistic regression analysis we identified CV risk factors: