level of tumor necrosis factor (TNF) and IL 1 β in the atorvastatin group, however, decrease was higher in IL6 and IL12p70 in the colchicine group. Mild diarrhea was reported as the most frequent adverse effect in the atorvastatin group of 3.33% and colchicine of 23.33% $p = 0.010$. There was a statistically significant decrease in cholesterol and LDL-cholesterol levels in favor of treatment with atorvastatin

Conclusion: We do not observe substantial differences in decrease in hs-cTnI with atorvastatin and colchicine, a prospective study of 222 patients is required to avoid β -type error. Echocardiographic abnormalities in 76% of patients showed a greater decrease in diastolic dysfunction in the atorvastatin group, as well as lower cholesterol and LDL-cholesterol levels, thus, as a tendency to falling of TNF and IL 1 β in this group

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FRI0051

RHEUMATOID ARTHRITIS PATIENTS WITH HIGH DISEASE ACTIVITY AND TREATED WITH HIGH DOSE GLUCOCORTICOID FREQUENTLY FALL: NINE YEARS OF THE TOMORROW STUDY

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Background: Falling is a multicausal phenomenon resulting from complex interactions between intrinsic and extrinsic or environmental factors. Patients with rheumatoid arthritis (RA) who have muscle weakness and stiff or painful joints might be at increased risk of falling. However, little is known about the exact properties of risk factors for falling in patients with RA. Recently, the disease activity of RA has been more satisfactorily controlled by the “treat-to-target” strategy, including the use of biologics. Given this new era, it is important to accurately estimate the incidence of falling in patients with RA and to elucidate contributing risk factors.

Objectives: The objective of this study was to evaluate the incidence of falling and associated risk factors in 208 patients with RA and in age- and sex-matched 205 controls (Co) who participated in the TOMORROW (TOtal Management Of Risk factors in Rheumatoid arthritis patients to IOW er morbidity and mortality) study, a 10-year cohort study that started in 2010 in Japan. This research was conducted using TOMORROW study data for 9 years.

Methods: We evaluated the incidence of falling by self-administered questionnaire every year and confirmed them by medical records. We also collected information about general health status, body composition including bone mineral density, lean body mass, fat mass and laboratory data. We compared the frequency of the incidence of falling in RA patients and Co for 9 years and analyzed risk factors for falling.

Results: A total of 157 patients with RA (mean age: 57.1 $\pm$ 12.5 years, female: 84.7%, mean disease duration 13.9 $\pm$ 12.0 years) and 169 Co (mean age: 57.6 $\pm$ 12.5 years, female: 84.0%) completed 9 years observation. The rate of individuals who fell did not differ between two groups (RA: 66.9%, Co: 59.2%, $p=0.19$). However, number of falls was higher in RA than Co (0.35 vs 0.21/person-year, $p=0.03$). Multivariate logistic regression analysis adjusted for age, sex and BMI, revealed that RA was not a risk factor for the incidence of falling (OR: 1.36, 95%CI: 0.8–2.32, $p=0.26$) and the history of falling was a risk factor for the incidence of falling (OR: 3.27, 95%CI: 1.78–7.0, $p<0.001$). Multivariate linear regression analysis adjusted for age, sex and BMI, revealed that mHAQ ($\beta=0.17$, $p=0.04$), mean DAS28-CRP over 9 years ($\beta=0.19$, $p=0.02$) and mean dosage of glucocorticoid over 9 years ($\beta=0.18$, $p=0.03$) were the risk factors for number of falls (table 1).

Table 1. Multivariate linear regression analysis of risk factors associated with number of falls sustained by patients RA.

		RA	N=157
		β	p
At the entry	Anti-CCP antibody (U/mL)	0.016	0.835
	RF (IU/ml)	0.020	0.803
	History of falling	0.103	0.201
	DAS28-CRP	0.078	0.333
	mHAQ	0.169	0.039
	Dose of GC (mg/day)	0.028	0.723
9 years	Average DAS28-CRP	0.185	0.024
	Average dose of GC (mg/day)	0.179	0.025

RA, rheumatoid arthritis; CCP, cyclic citrullinated peptide; RF, Rheumatoid factor; DAS28-CRP, disease activity score 28 with C-reactive protein; mHAQ, modified Health Assessment Questionnaire; GC, glucocorticoid.

Conclusion: There was no difference in the incidence of falling between RA and Co. However, number of falls was significantly higher in RA group. High disease activity and higher dosage of glucocorticoid were the risk factors for number of falls among RA patients.

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FRI0052

INFLUENCE OF RHEUMATOID ARTHRITIS ON THE CLINICAL AND BIOLOGICAL PROFILE OF TYPE-2 DIABETES MELLITUS

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Background: Type-2 diabetes and rheumatoid arthritis (RA) are two chronic diseases characterized by tissue inflammation and insulin resistance. To date, no data have evaluated the influence of RA-induced joint and systemic inflammation on the course of type-2 diabetes.

Objectives: To study the impact of RA on type-2 diabetes

Methods: Observational, multicenter, cross-sectional usual-care study, including 7 rheumatology centers. This study included over a 24-month period consecutive patients with type-2 diabetes and RA, fulfilling the 2010 ACR / EULAR criteria, and diabetic controls with osteoarthritis (OA). The following data were collected: demographics, disease activity and severity indices, current treatment for RA and diabetes, history and complications of diabetes. A systematic blood test was performed, assessing inflammatory (CRP levels) and metabolic (fasting glycemia and insulin levels, HbA1c) parameters. The HOMA2%B (insulin secretion) and HOMA2%S (tissue insulin sensitivity) indices (HOMA calculator, © Diabetes Trials Unit, University of Oxford) were used to assess insulin resistance. RA and OA

patients were compared using parametric tests after adjusting for age and BMI. A multivariate logistic regression was performed to identify factors independently associated with insulin resistance.

Results: We included 122 RA patients (74% women, mean age 64±11 years, mean disease duration 15±11 years, 75% with positive ACPA antibodies and 64% with erosive disease) and 54 controls with OA. 64% of RA patients were treated with oral corticosteroids <10mg/day, 65% received methotrexate and 53% received targeted biological therapies.

The characteristics of type-2 diabetes in the 54 OA patients corresponded to severe insulin-resistant diabetes: age > 65 years, high BMI > 30 kg/m², mean HbA1c 7.3%±1.1 1.3%, 30% of insulin requirement, high frequency of other cardiovascular risk factors, macroangiopathy found in almost half of patients and biological criteria of insulin resistance (elevation of HOMA2%B and decrease of HOMA2%S).

RA patients with type-2 diabetes had a younger age (64±11 years vs. 68±12 years, $p=0.031$) and lower BMI (27.7±11 5.5 vs. 31.5±11 6.3, $p<0.001$). These patients also had severe diabetes (HbA1c 7.0%±1.1 1.2%, 29% of insulin requirement, 43% of macroangiopathy) with an insulin resistance profile identical to OA controls. After adjusting for age and BMI, RA patients had a significantly increased insulin secretion compared to OA patients (HOMA2%B: 83.1±11 65.2 vs. 49.3±11 25.7, $p=0.023$) as well as a significant reduction of insulin sensitivity (HOMA2%S: 61.1±11 31.6 vs. 92.9±11 68.1, $p=0.016$). This insulin resistance was associated with the inflammatory activity of RA, with a negative correlation between the HOMA2%S and the DAS28 ($r=-0.28$, $p=0.027$). The multivariate logistic regression confirmed the independent association between the HOMA2%S index and DAS28 (OR: 3.93, 95% CI 1.02-15.06), as well as high blood pressure (OR: 1.29, 95% CI 0.33-1.99 CI).

Conclusion: RA patients with type-2 diabetes displayed severe, poorly controlled diabetes, highlighting the burden of comorbidities associated with RA. The clinical-biological profile of diabetic RA patients was severe insulin-resistant diabetes, with a biological profile of insulin resistance linked to the inflammatory activity of the disease. These findings may have therapeutic implications, with the potential targeting of insulin resistance through the treatment of joint and systemic inflammation.

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FRI0053

PROLIFERATIVE SYNOVITIS, AN ULTRASOUND PATTERN ASSOCIATED WITH ACPA POSITIVE RHEUMATOID ARTHRITIS

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Background: Seronegative (sero-) and seropositive (sero+) Rheumatoid Arthritis (RA) have different genetic, immunopathological and vascular morphology features, but no previous studies have analyzed if US characteristics differ between sero+ or sero- RA. Our preliminary studies suggest that sero+ RA is associated with an expansive synovitis pattern that we have called "proliferative synovitis" (PS)

Objectives: To analyze potential differences between patients with RA according to their autoantibody status by using ultrasonography (US). We aimed to assess whether PS is associated with ACPA+ pts

Methods: We collected clinical, epidemiological data and bilateral carpal and hand US images of pts with RA. Synovial hypertrophy (SH), Power Doppler signal (PD) and total score (sum of scores of SH and PD) in wrist and hand (1-5 metacarpophalangeal) were assessed. We evaluated the presence of PS, defined as expansive synovial growth encompassing the concepts of synovial SH grade II and III. We performed synovial biopsies of a subgroup of pts using arthroscopy or US guided in order to see immunohistochemistry differences between "proliferative" and "flat" (non-proliferative) synovitis. Serum levels of angiogenic and inflammatory biomarkers were performed

Results: Two hundred and five RA patients were collected. Overall, 173 (84.8%) pts were sero+ for RF (68.7%) or ACPA (74.6%), general characteristics are summarized in Table. No significant differences between sero+ and sero- pts in terms of disease activity or therapy were found. PS was present in 55.5% of sero+ pts (55.3% in RF+ and 58.2% in ACPA+ pts) and 16.1% of sero- pts ($p=0.0001$). Globally, 101 pts (49.2%) had PS. Ninety-six (95.0%) were RF or ACPA positive.

Only 5 pts with sero- RA had PS ($p=0.001$). In the univariate analysis, significantly more pts with PS had erosive disease (72.3% vs 35.0% $p=0.0001$), higher US scores ($p=0.0001$) and more of them were taking conventional synthetic Disease-modifying anti-rheumatic drugs (csDMARD) (81.8% vs 69.6% $p=0.05$). No differences regarding disease activity were found.

In the multivariate analysis erosions [OR 4.90 CI 95% (2.17-11.07) $p=0.0001$] and ACPA [OR 3.5 CI 95% (1.39-10.7) $p=0.09$] but not RF status [OR 0.74 CI 95% (0.31-1.71) $p=0.483$] were independently associated with the presence of PS.

We immunostained synovial biopsies from 23 pts with PS (13 pts) or non-PS (10 pts). PS was significantly associated with higher density of vessels ($p=0.042$) and a strong trend to a higher density of B, T, Mast cells and macrophages (figure 1). Significantly higher serum levels of angiogenic (Activin A, bFGF, IL18, IL20, PIGF, SDF-1 and VEGF-D) and pro-inflammatory (IL23) cytokines were found in patients with PS (figure 2).

Conclusion: The presence of "proliferative Synovitis" was significantly associated with ACPA and erosive disease in patients with RA. PS pattern also was associated with higher density of synovial vessels and higher serum levels of angiogenic and inflammatory mediators

Table.

	Total US pattern p value		
	N=205	Proliferative (N=101)	Non proliferative (N=104)
Female, n (%)	162 (79.4)	79 (78.2)	83 (80.6)
Age, mean (SD) years	57.1 (± 14.1)	56.3 (± 12.0)	58.0 (± 15.9)
Current Smoker, n (%)	47 (26.9)	22 (25.6)	25 (28.1)
Disease duration, mean (SD) months	113.3 (± 105.7)	127.7 (± 111.1)	99.3 (± 99.3)
Erosion, n (%)	108 (53.7)	73 (72.3)	35 (35.0)
ACPA, n (%)	153 (75.4)	89 (89)	64 (62.1)
RF, n (%)	99 (68.3)	78 (78)	63 (61.2)
DAS 28-CRP, mean (SD)	2.55 (±1.03)	2.66 (±1.04)	2.44 (±1.02)
GC, n (%)	99 (49.3)	45 (45.5)	54 (52.9)
csDMARDs, n (%)	152 (75.6)	81 (81.8)	71 (69.6)
bDMARD, n (%)	69 (34.3)	35 (35.4)	34 (33.3)
Total US score	14.9 (± 11.5)	18.8 (± 11.8)	11.1 (± 9.9)

*ACPA anti-citrullinated protein antibodies, RF rheumatoid factor, DAS28-CRP Disease Activity Score 28-joint count, CRP C-reactive protein, GC glucocorticoids, bDMARD biological disease-modifying antirheumatic drugs

Figure 1. Synovial cells density in 23 patients with RA.

Figure 2. Serum levels of angiogenic and inflammatory biomarkers in patients with RA.