Objectives: The objectives of this study were to: compare serum FGF-23 levels between RA patients and healthy controls and investigate possible associations between FGF23 as surrogate measures of cardiovascular disease.

Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. Total cholesterol and triglyceride levels were determined by fully enzymatic techniques. High-density lipoprotein (HDL) was determined after precipitation of apolipoprotein B (apoB)-containing lipoproteins with magnesium sulfate and dextran sulfate. Low-density lipoprotein (LDL) was calculated using the Friedewald formula. Serum FGF-23 was analyzed using ELISA.

Results: The mean serum total cholesterol, HDL-C, LDL-C, and triglycerides were 212.74±41 mg/dL, 69.92±19.45 mg/dL, 120.18±29.24 mg/dL and 112.93±55.67 mg/dL, respectively.

There was no significant differences in FGF-23 levels between the patients and controls [85.7 (5.2-275.4) vs. 81.2 (2.6-269.9), pg/ml; $P=0.4316$], but we found that FGF23 levels were positively associated with total cholesterol ($p < 0.05$), low-density lipoprotein (LDL-c) level ($p < 0.05$) and smoking ($p = 0.008$) in patients with RA.

Conclusion: We report an association between circulating FGF-23 and LDL-c in RA patients, representing a novel pathway linking high FGF23 to an increased cardiovascular risk.

REFERENCES:

- [1] Castañeda S, Nurmohamed MT, González-Gay MA. Cardiovascular disease in inflammatory rheumatic diseases. *Best Pract Res Clin Rheumatol*. 2016; 30(5):851-869.
- [2] Kendrick J, Cheung AK, Kaufman JS, Greene T, Roberts WL, Smits G, Chonchol M. FGF-23 associates with death, cardiovascular events, and initiation of chronic dialysis. *J Am Soc Nephrol*. 2011; 22(10):1913-1922.
- [3] Scialla JJ, Xie H, Rahman M, Anderson AH, Isakova T, Ojo A, et al. Fibroblast growth factor-23 and cardiovascular events in CKD. *J Am Soc Nephrol*. 2014; 25(2):349-360.
- [4] Mirza M, Alsiö J, Hammarstedt A, Erben RG, Michaëlsson K, Å Tivesten Å, et al. Circulating Fibroblast Growth Factor-23 Is Associated With Fat Mass and Dyslipidemia in Two Independent Cohorts of Elderly Individuals. *Arterioscler Thromb Vasc Biol*. 2011; 31:219-227.

Disclosure of Interests: Antonio Alvarez de Cienfuegos : None declared, Lucia Cantero-Nieto: None declared, José Alberto García-Gómez: None declared, Gema Robledo: None declared, Marta Trigo: None declared, Javier Martín Ibanez: None declared, Miguel A González-Gay Grant/ research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker's bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Norberto Ortego: None declared

DOI: 10.1136/annrheumdis-2019-eular.5076

THU0122 THE LACK OF EXERCISE HABIT WAS A RISK FACTOR FOR CLINICAL FRACTURES IN PATIENTS WITH RHEUMATOID ARTHRITIS -TOMORROW STUDY-

Shohei Anno^{1,2}, Kentaro Inui³, Yuko Sugioka⁴, Kenji Mamoto³, Tadashi Okano², Masahiro Tada⁵, Tatsuya Koike^{6,7}, Hiroaki Nakamura². ¹Osaka social medical center, Orthopaedic Surgery, Osaka, Japan; ²Osaka City University Graduate School of Medicine, Orthopaedic Surgery, Osaka, Japan; ³Osaka City University Graduate School of Medicine, Orthopaedic Surgery, Osaka, Japan; ⁴Osaka City University Graduate School of Medicine, Orthopaedic Surgery, Osaka, Japan; ⁵Osaka City General Hospital, Orthopaedic Surgery, Osaka, Japan; ⁶Osaka City University Graduate School of Medicine, Center for Senile Degenerative Disorders (CSDD), Osaka, Japan; ⁷Search Institute for Bone and Arthritis Disease (SINBAD), Osaka, Japan

Background: Patients with rheumatoid arthritis (RA) might be considered to be at increased risk of falls and fractures. However, little is known about the exact properties of risk factors for clinical fractures 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 clinical fracture in patients with RA and to elucidate contributing risk factors.

Objectives: The objective of this study was to evaluate the incidence of clinical fractures and associated risk factors in 208 patients with RA and in age- and sex-matched 205 controls (Cont) who participated in the TOMORROW (Total Management Of Risk factors in Rheumatoid arthritis patients to lower morbidity and mortality) study, a 10-year cohort study that started in 2010 in Japan. This research was conducted using TOMORROW study data for 7 years.

Methods: We evaluated the incidence of clinical fractures by self-administered questionnaire every year and confirmed them by medical records. We also collected information about daily walking time and weekly exercise time, general health status, body composition including bone mineral density, lean body mass, fat mass and laboratory data at baseline. We compared the frequency of the incidence of clinical fractures in RA patients and Cont for seven years and analyzed risk factors for clinical fractures in RA patients using multivariate regression analysis.

Results: A total of 208 patients with RA (mean age: 54.9 ± 10.1 years, female: 85.1%, mean disease duration 14.0 ± 11.8 years) and 205 Cont (mean age: 56.3 ± 10.4 years, female: 83.9%) were finally analyzed. The number of clinical fractures were no differences between RA and Cont group (RA: 47, Cont: 38, $p=0.37$). Comparing RA patients with or without the clinical fractures, age ($p=0.006$), disease duration ($p=0.005$), the average glucocorticoid dose ($p<0.001$), the average number of falls ($p<0.001$), and the average DAS28-ESR of seven years ($p=0.029$) were higher in patients with the incidence of clinical fractures. Multivariate logistic regression analysis revealed that RA was not a risk factor (OR: 0.655, 95%CI: 0.296 – 1.448, $p=0.296$), and the lack of exercise habit (OR: 2.221, 95%CI: 1.208-4.082, $p=0.001$) and glucocorticoid use (OR: 2.279, 95%CI: 1.036-5.015, $p=0.04$) were the risk factor for clinical fractures. Multivariate logistic regression analysis in RA patients, the lack of exercise habit represented an independent risk factor for the incidence of clinical fractures (OR: 4.466, 95%CI: 1.212-16.454, $p=0.025$).

Conclusion: Seven years of data from the TOMORROW cohort study including both RA patients and age- and sex-matched Cont showed no difference in the incidence rate of clinical fractures between RA and Cont groups. Multivariate logistic regression analysis revealed that RA was not a risk factor. However, the lack of exercise habit was significantly associated with an increased frequency of the incidence of clinical fracture among RA patients.

Acknowledgement: We wish to thank Atsuko Kamiyama, Tomoko Nakatsuka and the members of the Osaka City University hospital clinical research center.

Disclosure of Interests: Shohei Anno: None declared, Kentaro Inui Speakers bureau: Takeda Pharmaceutical, Pfizer Japan, Daiichi-Sankyo Co.Ltd., Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co.Ltd., Eli-Lilly, Nippon Kayaku Co.,Ltd., Maruho Co.,Ltd, Kaken Pharmaceutical Co.,Ltd., Yuko Sugioka: None declared, Kenji Mamoto: None declared, Tadashi Okano Speakers bureau: Abbvie, Masahiro Tada Speakers bureau: Abbvie, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical, Pfizer Japan, Takeda Pharmaceutical, Tatsuya Koike Speakers bureau: Abbvie, Astellas Pharma Inc., Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Hiroaki Nakamura: None declared

DOI: 10.1136/annrheumdis-2019-eular.3427

THU0123 FEMALES UNDERGO MORE TREATMENT CHANGES COMPARED TO MALES: ANALYSIS OF GENDER DIFFERENCES IN RHEUMATOID ARTHRITIS PATIENTS

ASTORRI DAVIDE¹, Francesca Ometto², Lara Friso³, Francesco Sartor³, Bernd Raffener⁴, Costantino Botsios⁵, Leonardo Punzi⁶, Andrea Doria³. ¹UNIVERSITY OF PADOVA, RHEUMATOLOGY UNIT, DEPARTMENT OF MEDICINE (DIMED), PADOVA, Italy; ²UNIVERSITY OF PADOVA, RHEUMATOLOGY UNIT, DEPARTMENT OF MEDICINE (DIMED), PADOVA, Italy; ³UNIVERSITY OF PADOVA, RHEUMATOLOGY UNIT, DEPARTMENT OF MEDICINE (DIMED), PADOVA, Italy; ⁴UNIVERSITY OF PADOVA, RHEUMATOLOGY UNIT, DEPARTMENT OF MEDICINE (DIMED), PADOVA, Italy; ⁵UNIVERSITY OF PADOVA, RHEUMATOLOGY UNIT, DEPARTMENT OF MEDICINE (DIMED), PADOVA, Italy; ⁶UNIVERSITY OF PADOVA, RHEUMATOLOGY UNIT, DEPARTMENT OF MEDICINE (DIMED), PADOVA, Italy

Background: Gender differences may contribute to treatment tailoring in rheumatoid arthritis (RA) patients. Observational data shows a trend toward worse disease activity and worse response to treatment in

females. Only few data are available specifically focused on differences in drug use according to gender.

Objectives: To evaluate gender differences in treatment approaches in RA patients treated with bDMARDs (biological DMARDs)

Methods: We included RA patients aged ≥ 18 years, with disease duration ≥ 1 years, with a stable bDMARD treatment (≥ 12 months) in a monocentric cohort in the North-East of Italy. Social, demographic, and clinical features in addition to treatments were considered. To assess variables independently associated with gender, all variables achieving a $p < 0.20$ in univariate analysis were included in a multivariate regression model.

Results: Among 721 RA patients, 514 patients were eligible for the analysis and 407 were females. Compared with males, females had a lower BMI, a higher DAS28, a higher number of conventional synthetic DMARDs (csDMARDs) used before the start of bDMARDs, a higher number of bDMARDs with different mechanism of action (MoA), a larger use of prednisone and a lower rate of combination with MTX (Table 1). After adjustment for confounding factors, females had an increased probability of taking ≥ 2 DMARDs before bDMARDs (OR 2.21, 95% CI 1.25-3.93, $p = 0.007$) and a lower BMI (per 5-unit increase, OR 0.70, 95% CI 0.56-0.87, $p = 0.001$) compared to males (Figure 1).

Conclusion: In a cohort of Italian RA patients, females were treated with a higher number of csDMARDs before starting a bDMARD compared to males and a trend toward the use of more bDMARDs with different MoA. Further insight is needed regarding possible differences in the accessibility to bDMARD treatment and reasons for unsatisfactory treatment control in females.

Variables included in multivariate analysis: Age, Disease duration, Positive RF and/or ACPA, BMI, ≥ 2 csDMARDs prior to bDMARDs, Disease activity (DAS28), Combination with MTX, PDN use, Time on bDMARDs, TNF inhibitors use, ≥ 2 Mechanisms of action of biological drugs

Abstract THU0123 – Figure 1

Abstract THU0123 – Table 1.

Characteristics of the patients in the entire cohort (514 patients) and according to gender		Univariate Analysis		Multivariate Analysis	
	All patients	Females	Males	p value	OR (95% CI)
Number	514	407	107	-	-
Females, n (%)	407 (79.2)	407 (100)	0 (0)	-	-
Positive RF or ACPA, n (%)	300 (58.4)	247 (60.7)	53 (49.5)	0.037	-
Age, years, median (IQR)	62.5 (53.7-70)	63 (53.7-71)	62 (51.5-68.5)	0.186	-
BMI, median (IQR)	23.88 (21.24-27.54)	23.38 (20.76-26.99)	25.93 (23.05-28.36)	0.001	per 5-unit increase (0.56;0.87)
Overweight, n (%)	210 (40.9)	149 (36.6)	61 (57)	<0.001	-
Disease duration, year, median (IQR)	18 (12-25)	18 (13-26)	17 (12-22)	0.122	-
Flammaroid, n (%)	24 (22.4)	24 (26.7)	0 (0)	0.016	-
Employed, n (%)	39 (41.5)	31 (39.2)	8 (53.3)	0.310	-
Education level, n (%)	11 (10.7)	11 (12.8)	0 (0)	0.486	-
Social status, n (%)	5 (6.2)	4 (6)	1 (7.1)	0.325	-
Smokers, n (%)	16 (18)	13 (17.1)	3 (23.1)	0.604	-
Distance from clinic, km, median (IQR)	37 (20.51-25)	35 (20.60)	40 (30.45)	0.943	-
No. of assessment per year, median (IQR)	4 (3-4)	4 (3-4)	3 (2.75-4)	0.087	-
High adherence to treatment, n (%)	50 (46.3)	39 (42.9)	11 (84.7)	0.097	-
csDMARDs prior to bDMARD treatment					
Number, median (IQR)	3 (2-3)	3 (2-3)	3 (2-3)	0.072	-
≥ 2 csDMARDs, n (%)	448 (87.2)	364 (89.4)	84 (78.5)	0.003	2.03 (1.13;3.63)
MTX, n (%)	496 (96.5)	399 (98)	97 (90.7)	<0.001	-
LFN, n (%)	221 (43)	184 (45.2)	37 (34.6)	0.048	-
SSZ, n (%)	139 (27)	105 (25.8)	34 (31.8)	0.215	-
HCO, n (%)	334 (65)	274 (67.3)	60 (56.1)	0.030	-
Other csDMARDs, n (%)	184 (35.8)	145 (35.6)	39 (36.4)	0.437	-
Disease assessment at the last follow-up visit					
DAS28, median (IQR)	0 (0-2)	0 (0-2)	0 (0-2)	0.842	-
SJC, median (IQR)	2 (2-4)	2 (2-4)	2 (2-4)	0.893	-
Physician-VAS, median (IQR)	40 (30-40)	40 (30-40)	40 (30-40)	0.970	-
CRP, mg/L, median (IQR)	5 (2-5)	5 (2-5)	5 (2-6.3)	0.113	-
DAS28, median (IQR)	3.09 (2.63-3.49)	3.1 (2.63-3.49)	2.99 (2.73-3.46)	0.855	-
Remission, n (%)	112 (21.8)	93 (22.9)	19 (17.8)	0.028	-
LDA, n (%)	198 (38.5)	147 (36.1)	51 (47.6)	0.002	-
MDA, n (%)	189 (36.8)	157 (38.6)	32 (29.9)	0.002	-
HAQ, n (%)	17 (3.3)	10 (2.5)	7 (6.5)	0.017	-
HAQ, median (IQR)	1.5 (1-1.8)	1.5 (1-1.8)	1.5 (1-1.8)	0.217	-
Physician-VAS, median (IQR)	35 (25-35)	35 (25-35)	35 (25-35)	0.873	-
SDAI, median (IQR)	11 (8-13.8)	11 (8-13.8)	10 (8-13.8)	0.786	-
CDAI, median (IQR)	10.5 (7.5-13.5)	10.5 (7.5-13.5)	9.5 (7.5-13.5)	0.802	-
csDMARDs associated with the bDMARD treatment					
MTX, n (%)	99 (19.3)	70 (17.2)	29 (27.1)	0.021	0.63 (0.38;1.06)
MTX dose, mg/week, median (IQR)	10 (10-10)	10 (10-10)	10 (10-10)	0.463	-
Subcutaneous/intramuscular vs oral	84 (80.4)	64 (61.5)	20 (57.1)	0.046	-
LFN, n (%)	29 (5.6)	26 (6.4)	3 (2.8)	0.153	-
SSZ, n (%)	3 (0.6)	2 (0.5)	1 (0.9)	0.592	-
HCO, n (%)	3 (0.6)	3 (0.7)	0 (0)	0.373	-
Other csDMARD, n (%)	2 (0.4)	2 (0.5)	0 (0)	0.468	-
Combination with MTX and/or LFN, n (%)	128 (24.9)	96 (23.6)	32 (29.9)	0.179	-
PDN use, n (%)	319 (62.1)	261 (64.1)	58 (54.2)	0.060	1.55 (0.99;2.43)
PDN dose, mg/day, median (IQR)	2.5 (0.5)	2.5 (0.5)	2.5 (0.5)	0.176	-
NSAIDs use, n (%)	43 (8.5)	33 (8.2)	10 (10.3)	0.699	-
bDMARD treatment					
Time on treatment, years, median (IQR)	10.05 (5.96-13.05)	10.13 (6.43-13.21)	9.72 (3.96-12.63)	0.106	-
Disease duration at the start, median (IQR)	8.1 (3.88-14.1)	8.3 (4.15)	8 (3.3-12)	0.205	-
Number (ever), median (IQR)	2 (1-2)	2 (1-2)	1 (1-2.5)	0.431	-
TNF-inhibitors use (ever), n (%)	482 (93.8)	378 (92.9)	104 (97.2)	0.100	-
MDA number (ever), median (IQR)	1 (1-2)	1 (1-2)	1 (1-2)	0.179	-
≥ 2 MDA, n (%)	118 (36.6)	117 (38.6)	31 (29)	0.066	-
Current subcutaneous vs. endovenous administration, n (%)	449 (87.4)	354 (87)	95 (88.8)	0.617	-

IQR, inter-quartile range; MTX, methotrexate; LFN, leflunomide; SSZ, sulfasalazine; HCO, hydroxychloroquine; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs, biological DMARDs; SJC, swollen joint count; CRP, C-reactive protein; DAS28, disease activity score 28; LDA, low disease activity; MDA, moderate disease activity; HAQ, high disease activity; HAQ, health assessment questionnaire; SDAI, simplified disease activity index; CDAI, clinical disease activity index; PDN, prednisone; NSAIDs, non-steroidal anti-inflammatory drugs; MDA, mechanism of action; TNF-inhibitors, tumor necrosis factor inhibitors; "data available in 107 patients; "adherence measured with the Italian validated Sitem Compliance Questionnaire for Rheumatology (i-CORSY)¹⁶."

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3784

THU0124

INFLUENCE OF AUTOIMMUNE VASCULITIS ON LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

Miklós Bély^{1,1}, Ágnes Apáthy². ¹Hospital of the Order of the Brothers Saint John of God in Budapest, Department of Pathology, Budapest, Hungary; ²St. Margaret Clinic, Budapest, Department of Rheumatology, Budapest, Hungary

Background: Complications of rheumatoid arthritis (RA) may modify the clinical course and symptoms of allied disorders leading to missed diagnosis or late recognition of associated diseases.

Objectives: The aim of this study was to determine the possible role of classic complications of RA: systemic autoimmune vasculitis (AV), AA amyloidosis (AAa), lethal cardiac insufficiency (CI) caused by endo-, myo- or pancarditis, with or without interstitial pneumonitis, furthermore lethal septic infection (SI) on prevalence and mortality of coexistent associated diseases: atherosclerosis (Ath), hypertension (HT), type 2 diabetes mellitus (DM), and tuberculosis (Tb) with miliary dissemination (mTb).

Methods: 234 non-selected autopsy patients with RA were studied. RA was confirmed clinically according to the criteria of the ARA.

The presence of AV, AAa, CI and SI was determined at autopsy and confirmed by a detailed review of extensive histological material. The prevalence and mortality of associated diseases Ath, HT, DM, Tb or mTb were determined and analyzed retrospectively, reviewing the clinical and pathological reports.

The link between AV, AAa, CI or SI and Ath, HT, DM, Tb or mTb was analyzed by (χ^2) test.

Results: RA was complicated by AV in 43 (18.4%), by AAa in 48 (20.5%), by CI in 15 (6.4%), and by lethal SI in 33 (14.1%) of 234 patients.

RA associated with severe Ath in 106 (45.3%), with HT in 41 (17.5%), with DM in 41 (17.5%), with Tb in 28 (11.9%) and with mTb in 9 (3.8%) of 234 patients.

As a basic disease Ath led to death in 61 (26.1% of 106), HT in 2 (0.9% of 41), DM in none (0% of 41) and Tb with mTb in 3 (1.3% of 28) of 234 patients. Tb without miliary dissemination was not lethal in our patient population.

The statistical links ("p" values of significance) between complications of RA and prevalence or mortality of allied disorders are summarized in Table. (*asterisk indicates a negative value of associations' coefficient with inverse relationship).

Complications of RA	AV n=43 of 234	AAa n=48 of 234	CI n=15 of 234	SI n=33 of 234
Allied disorders in RA				
Ath n=106 of 234	$\chi^2=6.43^*$, p<0.01	$\chi^2=10.04^*$, p<0.001	$\chi^2=0.92^*$, p<0.33	$\chi^2=5.03^*$, p<0.02
Ath lethal n=61 of 106	$\chi^2=15.92^*$, p<0.001	$\chi^2=11.04^*$, p<0.001	$\chi^2=4.29^*$, p<0.03	$\chi^2=12.01^*$, p<0.001
HT 41 of 234	$\chi^2=3.20^*$, p<0.07	$\chi^2=0.03^*$, p<0.86	$\chi^2=0.00^*$, p<0.92	$\chi^2=1.27^*$, p<0.25
HT lethal n=2 of 41	$\chi^2=0.05^*$, p<0.80	$\chi^2=0.02$, p<0.87	$\chi^2=1.16^*$, p<0.28	$\chi^2=0.19^*$, p<0.65
DM 41 of 234	$\chi^2=0.05^*$, p<0.81	$\chi^2=1.05^*$, p<0.30	$\chi^2=0.92$, p<0.33	$\chi^2=0.01$, p<0.91
Tb 28 of 234	$\chi^2=4.02$, p<0.04	$\chi^2=2.61^*$, p<0.10	$\chi^2=0.33$, p<0.56	$\chi^2=0.37$, p<0.54
Tb lethal n=3 of 28	$\chi^2=0.00^*$, p<0.93	$\chi^2=0.02^*$, p<0.86	$\chi^2=0.53^*$, p<0.46	$\chi^2=0.01^*$, p<0.89
mTb 9 of 28	$\chi^2=4.24$, p<0.03	$\chi^2=0.08$, p<0.77	$\chi^2=0.01$, p<0.91	$\chi^2=0.05$, p<0.82
mTb lethal n=3 of 9	$\chi^2=0.00^*$, p<0.93	$\chi^2=0.02^*$, p<0.86	$\chi^2=0.53^*$, p<0.46	$\chi^2=0.01^*$, p<0.89

Conclusion: The inverse correlations between AV, AAa, CI, SI and Ath, HT, DM, Tb or mTb indicate that the prevalence and mortality of allied disorders were not influenced basically by the complications of RA.

The consequently inverse and (in most cases) significant correlations between prevalence of AV, AAa, CI, SI and the prevalence and mortality of Ath show that these are independent entities in RA. The AV, AAa, CI and SI are the most important complications of RA, and are characterized severe forms of disease, mostly involving younger patients, with an earlier onset (without pronounced atherosclerosis); while Ath is basically an age dependent phenomenon, characteristically present in RA patients with advanced age. RA patients with Ath may represent a special group of RA, characterized by lower incidence of AV, AAa, CI or SI, and a better prognosis.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.604