Rheumatoid arthritis - comorbidity and clinical aspects

AB0236 PRESENCE OF ANTI-CITRULLINATED POLYPEPTIDE ANTIBODIES DECREASES BONE MINERAL DENSITY IN BODY OF PATIENT WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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Background: Presence of anti-citrullinated polypeptide antibodies (ACPA) is one risk factor of bone erosion of the joint in patients with rheumatoid arthritis (RA). However, bone absorption in the whole body is still not clarified in a longitudinal study.
Objectives: The aim of this study is to clarify effects of ACPA on bone mineral density (BMD) decrease using dual-energy X-ray absorptiometry (DXA) in patient with RA using retrospective longitudinal cohort study.
Methods: Patient with RA who were measured BMD in lumbar spine (LS) and total hip (TH) using dual-energy X-ray absorptiometry (DXA) at first consultation (baseline) and were treated for more than five years, were recruited. Follow-up started at BMD measurement and continued until the development of the first fracture or censoring at death, loss to follow-up or end of the study. Every patients have been followed up with monitoring of SDAI and Health Assessment Questionnaire Disability Index (HAQ) at every another to three months. Sharp/van der Heijde Score (SHS) was measured at baseline and every another year thereafter. BMD were measured every six months. Relationship between BMD and candidate risk factors including ACPA positivity and serum titer level, and other variants for BMD loss were evaluated statistically using linear regression analysis. Evaluations were performed for the absolute value of BMD and Z-score at baseline, mean value of these during follow-up, and change from baseline. Change of Z-score during follow-up was also compared between groups what classified according to ACPA positivity (ACPA positive/negative group).
Results: A total of 222 patients were recruited including 17 male (7.7%) and 205 female (92.3%). The mean age of the patients was 69.2 years old. Mean disease duration at baseline and follow-up length after baseline were 6.4 and 63.3 months, respectively. Mean SDAI score, HAQ score and SHS at baseline were 22.2, 0.516, and 6.6, respectively. The mean ACPA level and positive rate were 202.1 and 77.5%, respectively.
Higher ACPA titer level correlated significantly low BMD and Z-score in TH ($p<0.05$), whereas ACPA positivity significantly correlated with low Z-score in LS and TH during follow-up using univariate models ($p<0.05$). The ACPA positivity also correlated with decrease of Z-score in both LS and TH using univariate models ($p<0.05$), whereas no significant correlation demonstrated using multivariate model.
Change of Z-score in the ACPA positive group was significantly lower than in the ACPA negative group despite no significant difference of disease activity between the two groups demonstrated ($p<0.05$) (Table 1).

Table 1. Comparison of the two groups

	parameters	ACPA-positive (n=172)	ACPA-negative (n=50)	p-value
	female (%)	91.3	96.5	0.10
at baseline	age (year-old)	65.4	71.3	**<0.001**
	disease duration (months)	7.7	4.6	**<0.001**
	RF (IU/L)	138.3 (197.1)	21.5 (49.3)	**<0.001**
	SDAI	26.3 (24.0)	21.0 (17.8)	**<0.05**
	HAQ	0.496 (0.618)	0.553 (0.639)	0.48
	SHS	8.4 (8.2)	3.5 (5.0)	**<0.001**
	BMD in LS (g/cm2)	0.825 (0.167)	0.849 (0.156)	0.23
	BMD in H (g/cm2)	0.700 (0.140)	0.710 (0.132)	0.75
	Z-score in LS	-0.246 (1.300)	0.123 (1.392)	**<0.05**
	Z-score in TH	-0.062 (1.034)	0.261 (1.020)	**<0.05**
at follow-up	follow-up length (months)	64.8	65.4	0.65
	SDAI	4.5 (3.1)	5.1 (4.4)	0.22
	HAQ	0.495 (0.616)	0.516 (0.544)	0.32
	SHS	8.1 (8.2)	3.4 (4.8)	**<0.001**
	BMD in LS (g/cm2)	0.839 (0.171)	0.870 (0.165)	0.16
	BMD in TH (g/cm2)	0.710 (0.118)	0.713 (0.115)	0.99
	Z-score in LS	-0.008 (1.361)	0.368 (1.426)	**<0.05**
	Z-score in TH	0.129 (0.902)	0.396 (0.891)	0.11
	anti-osteoporotic drug administered, ever (%)	73.4	69.8	0.72
	GCS administered, ever (%)	35.8	32.9	0.68

The values are presented as mean (SD) unless indicated otherwise.Statistically significant within 0.05 are shown as bold styles.

Conclusion: Presence of ACPA potentially have an independent risk of BMD decrease. Its action affects regardless gender and age.

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AB0237 CHANGES AND CLINICAL SIGNIFICANCES OF PERIPHERAL REGULATORY T CELLS IN RHEUMATOID ARTHRITIS PATIENTS WITH CARDIOVASCULAR DISEASE

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Background: Rheumatoid arthritis (RA) is an independent risk factor for cardiovascular diseases (CVD), driven by the underlying chronic systemic inflammation [1]. The imbalance of $CD4^+$ T lymphocyte subsets, especially between T helper (Th) 17 cells and regulatory T (Treg) cells, can mediate autoimmune inflammatory process, promoting the overproduction of cytokines and abnormal antibodies [2,3]. However, the levels of peripheral Th17 and Treg cells in RA patients with CVD are still unknown.
Objectives: To explore the expression of circulating Th17 and Treg cells in RA patients with CVD and analyze its clinical significance.
Methods: A total of 192 patients with RA and 86 healthy controls (HCs) were enrolled from January 2019 to January 2021. The peripheral blood $CD4^+$T lymphocyte subsets of all participants were assessed by flow cytometry. Patients were divided into RA-CVD group (n=72) and RA only group (n=120), and the clinical data were recorded. The statistical differences between two groups were analyzed by independent-samples *t* test, χ^2 test or Mann-Whitney *U* test, and risk factors of CVD were analyzed using Logistic regression.
Results: ① The median age and the percentage of male patients in the RA-CVD group were significantly higher than those in the RA only group. ② The absolute numbers of peripheral Treg cells in the patients with RA only and RA-CVD were all significantly lower than those in HCs [24.94 (19.32, 34.12) cells/μl *vs.* 33.13 (24.96, 45.83) cells/μl , Z=-4.135 , $P<0.01$; 19.13 (13.76, 27.34) cells/μl *vs.* 33.13 (24.96, 45.83) cells/μl , Z=-5.354 , $P<0.01$]. While the numbers of peripheral Th17 cells in two groups of patients were not significantly different with those in HCs. The ratios of Th17/Treg cells in two group patients were higher than those of HCs, but only the difference between RA-CVD patients and HCs were significant [0.40 (0.23 , 0.63) *vs.* 0.18 (0.13 , 0.29) , Z=-4.696 , $P<0.01$]. ③ Compared to the RA only patients, the absolute counts of Treg cells in RA-CVD patients were significantly lower [Z=-3.047 , $P<0.01$], the numbers of Th17 cells were significantly higher [7.48 (3.72, 13.63) cells/μl *vs.* 5.59 (3.49 , 8.91) cells/μl , Z=-1.989 , $P<0.05$], and the ratio of Th17/Treg cells was significantly higher [0.40 (0.23 , 0.63) *vs*. 0.23 (0.14 , 0.35) , Z=-4.289 , $P<0.01$]. ④ Logistic regression analysis showed that the level of circulating Treg cells (*OR*=0.936, 95%*CI*: 0.906-0.968) was a protective factor, while Th17 cells (*OR*=1.068, 95%*CI*: 1.020-1.119), elder age (*OR*=1.039, 95%*CI*: 1.004-1.076) and hypertension (*OR*=2.712, 95%*CI*: 1.254-5.865) were independent risk factors of RA patients complicated with CVD.
Conclusion: It is suggested that the immune imbalance caused by the deficiency of Treg cells may be involved in the occurrence and development of RA complicated with CVD, and to restore Treg numbers and function may be a promising preventive strategies.
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AB0238 HEALTH-RELATED QUALITY OF LIFE AND CORRELATION WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with active rheumatoid arthritis (RA) are at risk for poor functional outcomes, affecting quality of life (QoL). SF-36 is a validated instrument to measure health-related quality of life (HRQoL) in various domains of physical and mental health[1], and has been validated in RA. Nevertheless,

data on the impact of RA disease activity on SF-36 scores in Greek patients are lacking.

Objectives: To compare SF-36 scores in Greek RA patients versus the general population and to assess the impact of disease activity on HRQoL.

Methods: Cross-sectional study in RA patients followed in the Department of Rheumatology, Asklepieio Voulas General Hospital (05-10/2021). Demographic characteristics, state of disease activity and current treatment for RA were recorded at most recent visit. All patients completed SF-36 questionnaires and were classified in three subgroups of DAS28-disease activity: i) Remission or Low disease activity (LDA), ii) Moderate disease activity (MDA), and iii) High disease activity (HDA). Data from the SF-36 validation study in the Greek general population with 1007 participants, were used as historical controls[2]. Descriptive statistics, one-way ANOVA and linear regression were used for statistical analyses.

Results: 107 patients participated in the study (80,4% females, mean (SD) age 63.3 (12.1) years, 64.5% seropositive, 72% overweight or obese). One third (n=36) were active smokers and 63% (n=67) were receiving a biologic disease modifying antirheumatic drug (bDMARD).

Patients with RA exhibited low scores in all SF-36 domains and reported significantly worse results compared to the general population (Figure 1).

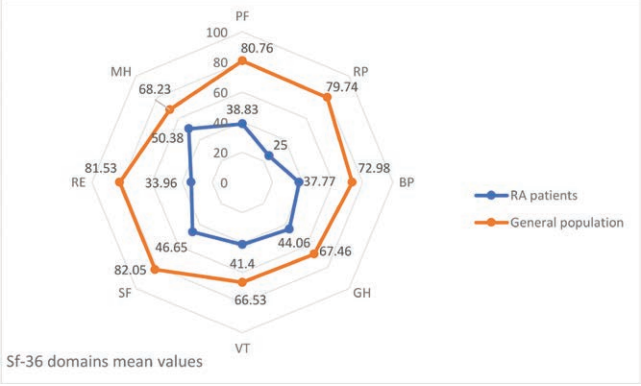

Figure 1.

Physical component score (PCS) and Mental component score (MCS) of the SF-36 showed a negative correlation with DAS28 (β= -8.28, p= <0.001 and β= -6.2, p= <0.001, respectively). Patients with remission or LDA exhibited better SF-36 scores compared to the other subgroups; moreover, patients with MDA had better SF-36 scores than those with HDA (Table 1). When patients with MDA were further divided into low- and high-moderate disease activity (DAS28: 3,21-4,19 and 4,2-5,1, respectively), no significant difference in any SF-36 domain was found between the two groups.

Table 1.

SF-36 domain mean±SD	RDA or LDA 51%	MDA 37,2%	HAD 11,7%	p-value
PF	48,43 ±34,23	32,14 ±19,83	20 ± 19,75	**0.003**
RP	34,9 ±43,68	20,71 ± 32,92	0 ± 0	**0.015**
BP	51,2 ±30,47	28,24 ± 24,49	18,86 ± 23,54	**<0.001**
GH	48,83 ±45	41,57 ± 24,25	32,27 ± 19,54	**0.043**
VT	49,48 ±22,22	34,14 ± 18,57	30,91 ± 15,94	**0.001**
SF	52,16 ±35,33	40,36 ± 27,13	28,41 ± 14,89	**0.041**
RE	39,01 ±44,68	27,62 ± 40,81	18,18 ± 34,52	0.246
MH	54,08 ±23,24	47,57 ± 21,75	40 ± 18,59	0.124

Conclusion: HRQoL assessed by SF-36 is dampened in RA patients, in both physical and mental component. Disease activity had a negative impact on both physical and mental components of HRQoL. Patients with remission or LDA showed better HRQoL outcomes, suggesting that the treat-to-target approach may also positively affect QoL.

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AB0239 **HOW SOLID MALIGNANCIES ARE DETECTED IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS**

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Background: According to a meta-analysis reported in 2015[1], among solid malignancies (cancers), only lung cancer was at an increased risk in patients with rheumatoid arthritis (RA) compared with the general population. A Japanese cohort study reported that the incidence of cancers in patients with RA treated with biological DMARDs was not significantly elevated compared to the Japanese general population[2]. However, in recent years, malignancy has been one of the major causes of death in Japanese patients with RA[3]. It has been reported that there was an increased incidence of malignancies in patients treated with tofacitinib compared to TNF-alpha inhibitors. Clinicians need to pay more attention to emerging malignancies.

Objectives: We explored how to detect cancer early in patients attending rheumatology outpatient clinics.

Methods: In this retrospective study, we studied 545 patients with RA who visited our rheumatology clinic between April 2011 and December 2021. Forty-five cases of cancer in 38 patients (31 women, 7 men) with RA were reviewed.

Results: Cancer types: 9 breast, 8 lung, 6 colon, 5 uterus, 4 stomach, 2 prostate, 2 pancreas and 9 others. Five female patients had metachronous or simultaneous double cancers and one male patient had metachronous triple cancers. The median age at diagnosis of 45 cancers was 72 years old (IQR 63–76.5) and the median duration of RA prior to cancer diagnosis was 10 years (IQR 5–20.5).

Lung: Seven cases were found by chest CT at the outpatient clinics; two at the start of bDMARDs and five during RA treatment.

Stomach and Colon: Two cases of four stomach cancers were discovered due to the progression of anemia. Both patients were at an advanced stage with distant metastasis and died 2 months after diagnosis. On the other hand, four of six colon cancers were detected by the fecal occult blood test, and three were in remission.

Of the 45 cases, only 8 cases were detected by cancer screening. In 15 cases, blood samples or imaging tests were the triggers cancer detection. Eight of the 15 cases were detected by routine examinations in the rheumatology outpatient clinic, but five cases were already in the advanced stage.

Table 1. Forty-five cancers in 38 patients with rheumatoid arthritis

		Clue to cancer diagnosis and prognosis at the final visit (death - under treatment - remission)					
Site of cancer	n	noticing symptoms		Various tests in outpatient clinic symptoms(-)		Cancer Screening	
Breast	9	8	(1-4-3)			1	(0-0-1)
Lung	8	1	(1-0-0)	7	(2-3-2)		
Colon	6			1	(1-0-0)	5	(0-1-4)
Stomach	4	1	(0-0-1)	3	(3-0-0)		
Cervix uteri	3	1	(0-0-1)			2	(0-0-2)
Corpus uteri	2	2	(0-2-0)				
Pancreas	2			2	(0-2-0)		
Prostate	2	2	(0-1-1)				
Skin*	2	2	(0-0-2)				
Oral/throat	2	2	(0-2-0)				
Duodenum	1	1	(0-0-1)				
Biliary tract	1	1	(0-1-0)				
Anus	1					1	(0-0-1)
Bladder	1			1	(0-0-1)		
Brain	1			1	(0-1-0)		
Total	45	21	(2-10-9)	15	(6-6-3)	9	(0-1-8)

Conclusion: We have been performing cancer screening before RA treatment and performing routine blood, urine, and imaging tests to identify adverse effects. However, they cannot always find cancers at the early stage. Screening procedures for malignancy are strongly recommended[4], but the consultation rates for breast and cervical cancer screening are lower in Japan than in European nations. We should encourage our patients to undergo usual age- and sex-appropriate cancer screening.

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