

# Temporomandibular joint involvement in elderly onset and young onset rheumatoid arthritis patients

Manolya Ilhanli<sup>1\*</sup> , Ilker Ilhanli<sup>2</sup> 

## SUMMARY

**OBJECTIVE:** There are studies showing clinical and laboratory differences between elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis. Temporomandibular joint involvement in rheumatoid arthritis is not rare. In this study, we aimed to examine the temporomandibular joint involvement and magnetic resonance imaging findings in elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis patients.

**METHODS:** A total of 87 rheumatoid arthritis patients were investigated retrospectively. The onset  $\geq 60$  years was considered elderly-onset rheumatoid arthritis. Erosion, flattening, and resorption of the condyle, narrowing of the joint space, joint effusion, synovial hypertrophy, and synovitis were interpreted as temporomandibular joint involvement with magnetic resonance imaging. Patients' age, gender, rheumatoid factor, and anti-cyclic citrullinated peptide positivity, extra-articular findings, medical treatment, and disease activity score were noted.

**RESULTS:** A total of 15 (17.2%) patients had elderly-onset rheumatoid arthritis. Temporomandibular joint involvement was detected in 67 (77%) patients; 9 (60%) of them were in the elderly-onset rheumatoid arthritis group (n=15) and 58 (80.6%) of them were in the young-onset rheumatoid arthritis group (n=72). Patients with temporomandibular joint involvement were significantly higher than those without temporomandibular joint involvement in both the elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis groups ( $p < 0.001$ ). No significant difference was found between elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis for the temporomandibular joint involvement ( $p = 0.100$ ). In the young-onset rheumatoid arthritis group, rheumatoid factor positivity and anti-cyclic citrullinated peptide positivity were more frequent in the patients with temporomandibular joint involvement ( $p = 0.011$ ,  $p = 0.024$ ). A comparison of the elderly-onset rheumatoid arthritis and young-onset rheumatoid arthritis patients showed no significant difference in the magnetic resonance imaging findings except for the resorption of the condyle.

**CONCLUSION:** According to our findings, elderly-onset rheumatoid arthritis is not much different from young-onset rheumatoid arthritis in terms of temporomandibular joint involvement, magnetic resonance imaging findings, and clinical and laboratory features.

**KEYWORDS:** Elderly. Rheumatoid arthritis. Temporomandibular joint.

## INTRODUCTION

Although there are no clinical findings, rheumatoid arthritis (RA) is a disease in which subclinical inflammation continues<sup>1</sup>. The prevalence of RA is known to be 0.5–1%<sup>2</sup>. Although RA can be diagnosed in all age groups and in all ethnic populations, it has an increasing prevalence with increasing age, and this frequency rises to 2% in the geriatric population<sup>3</sup>.

The terminology is unclear; however, patients with RA whose clinical symptoms begin after the age of 60 or 65 years are considered elderly-onset RA (EORA)<sup>3,4</sup>. As life expectancy increases in developed countries, the number of people  $\geq 60$  years old is increasing rapidly; this indicates that the number of EORA patients will increase in the future<sup>5</sup>. There are studies showing clinical and laboratory differences between EORA and young-onset RA (YORA)<sup>6</sup>.

The temporomandibular (TMJ) joint is a synovial joint formed between the mandible and the temporal bones. Problems related to TMJ have been reported as the second most common complaint after low back pain<sup>7</sup>. Since RA is an inflammatory arthritis involving synovial joints, it is not surprising that it involves TMJ. The incidence of TMJ involvement in RA patients ranges from 5 to 86%<sup>8</sup>. In this study, we aimed to examine the TMJ involvement and magnetic resonance imaging (MRI) findings in EORA and YORA patients.

## METHODS

A total of 99 patients who were followed up in the rheumatology clinic and diagnosed with RA according to the 2010 American College of Rheumatology-Rheumatoid Arthritis

<sup>1</sup>Giresun University, Health Application and Research Center – Giresun, Turkey.

<sup>2</sup>Ondokuz Mayıs University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation – Samsun, Turkey.

\*Corresponding author: manolya\_dmrnc@hotmail.com

Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.

Received on April 06, 2023. Accepted on May 21, 2023.

This study was carried out at Ondokuz Mayıs University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Division of Rheumatology, Samsun, Turkey.

(ACR-RA) classification criteria<sup>9</sup> and who were examined due to the TMJ complaints in the dental clinic between January 2020 and July 2022 were retrospectively analyzed. The records of patients with consent were reviewed. Those under the age of 18 years, without consent, and those who did not have an MRI were excluded from the study. The onset age of  $\geq 60$  was accepted as EORA and those  $< 60$  were considered as YORA<sup>4</sup>.

Patients' age (years) and gender were recorded. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) values were obtained. RF and anti-CCP tests were considered positive or negative based on laboratory reference values<sup>9</sup>. Those who had extra-articular findings accompanying RA were noted. Steroid and disease-modifying anti-rheumatic drugs (DMARDs: methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, biologics) usage were investigated. Disease activity scores calculated with erythrocyte sedimentation rate (DAS 28) values were noted.

Erosion, flattening, and resorption of the condyle, narrowing of the joint space, joint effusion, synovial hypertrophy, and synovitis were interpreted as TMJ involvement with MRI<sup>10</sup>.

It was decided whether the data were normally distributed or not by evaluating the skewness and kurtosis values and normality plots<sup>11</sup>. Mean and standard deviation values were given for normally distributed data, and median and minimum-maximum

values were given for non-normally distributed data. Mann-Whitney U test was used to compare non-normally distributed data, while the t-test was used for normally distributed data. Chi-square and Fisher's exact tests were used to determine the difference between the two groups. Kruskal-Wallis test was used to determine the difference of more than two between the groups. Significance level was accepted as  $p < 0.05$ . SPSS version 22 was used for statistical analysis (SPSS Inc., IBM Co., and Chicago, IL, USA).

The study protocol was approved by the Ondokuz Mayıs University Faculty of Medicine ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

## RESULTS

A total of 4 patients without consent and 12 patients who did not have MRIs were excluded. Overall, 87 patients were included in the study, 9 of whom were males (10.3%). The mean age of the patients was  $48.56 \pm 13.98$  years. The disease duration was  $80.59 \pm 56.79$  months. Notably, 15 (17.2%) patients had EORA; TMJ involvement was detected in 67 (77%) patients, 9 (60%) of them were in the EORA group ( $n=15$ ) and 58 (80.6%) of them were in the YORA group ( $n=72$ ) (Table 1).

**Table 1.** Comparison of elderly-onset and young-onset rheumatoid arthritis patients.

	EORA, n=15	YORA, n=72	p-value
Age (years)	67.4 $\pm$ 3.31	44.64 $\pm$ 12	<0.001*
Gender, male (%)	3 (20)	6 (8.33)	0.182
Disease duration (months)	40.2 $\pm$ 23.91	89 $\pm$ 58.12	0.002*
DAS 28	3.72 $\pm$ 1.43	3.59 $\pm$ 1.33	0.590
TMJ involvement (%)	9 (60)	58 (80.6)	0.100
RF positive (%)	3 (20)	32 (44.4)	0.079
Anti-CCP positive (%)	6 (40)	40 (55.6)	0.272
Rheumatoid nodule positive (%)	1 (6.7)	4 (5.6)	1.000
Methotrexate+glucocorticoid (%)	1 (6.7)	4 (5.6)	0.943
Methotrexate+sulfasalazine (%)	9 (60)	41 (56.9)	
Leflunomide (%)	1 (6.7)	3 (4.2)	
Biologics (%)	4 (26.7)	24 (33.3)	
Erosion (%)	9 (60)	52 (72.2)	0.365
Resorption of the condyle (%)	7 (46.7)	10 (13.9)	0.008*
Flattening of the condyle (%)	6 (40)	28 (38.9)	0.936
Narrowing of the joint space (%)	4 (26.7)	24 (33.3)	0.765
Joint effusion (%)	1 (6.7)	18 (25)	0.174
Osteophytes (%)	7 (46.7)	44 (61.1)	0.301
Disk perforation (%)	0	8 (11.1)	0.341

Significance level \* $p < 0.05$ ; n: number of subjects; EORA: elderly-onset rheumatoid arthritis; YORA: young-onset rheumatoid arthritis; DAS 28: disease activity score 28; TMJ: temporomandibular joint; RF: rheumatoid factor; anti-CCP: anti-cyclic citrullinated peptide.

Patients with TMJ involvement were significantly higher than those without TMJ involvement in both the EORA and YORA groups ( $p < 0.001$  for each).

The age of EORA patients was significantly higher ( $p < 0.001$ ), and disease duration was significantly lower ( $p = 0.002$ ) than that of YORA patients (Table 1). Although the number of patients who had TMJ involvement was numerically higher in the YORA group, no statistically significant difference was found between EORA and YORA for TMJ involvement ( $p = 0.100$ , Table 1).

In the EORA group with TMJ involvement, disease duration was significantly shorter ( $p = 0.004$ ). In the YORA group, patients with TMJ involvement were significantly older than patients without TMJ involvement ( $p = 0.001$ ). Also, in the YORA group, RF positivity and anti-CCP positivity were more frequent in patients with TMJ involvement ( $p = 0.011$  and  $p = 0.024$ ). Comparisons of the patients with and without TMJ involvement are shown in Table 2.

Comparison of the EORA and YORA patients showed no significant difference in the MRI findings except for the resorption of the condyle (Table 1). Comparisons of the patients with and without TMJ involvement according to MRI findings are shown in Table 3.

## DISCUSSION

In our study, all the patients had TMJ complaints. According to the MRI findings, we detected TMJ involvement in 67 (77%) patients. Patients with TMJ involvement were significantly higher than those without TMJ involvement in both the EORA and YORA groups. TMJ problems can affect up to 5–12% of the entire population<sup>12</sup>. There are no data about the comparison of EORA and YORA for TMJ complaints. EORA is associated with higher disease activity and accelerated joint destruction compared with YORA<sup>6</sup>. Although TMJ involvement is numerically found to be higher in YORA patients than in

**Table 2.** Comparison of the patients with and without temporomandibular joint involvement according to demographic, clinical, and laboratory findings.

		EORA		YORA		p-value
		TMJ involvement positive n=9	TMJ involvement negative n=6	TMJ involvement positive n=58	TMJ involvement negative n=14	
Age (years)		67±3.87 <sup>ab</sup>	68±2.44 <sup>cd</sup>	46.93±11.18 <sup>bde</sup>	35.14±10.83 <sup>ace</sup>	<0.001*
		p=0.586		p=0.001*		
Gender	Male	3	0	6	0	0.062
	Female	6	6	52	14	
		p=0.229		p=0.589		
Disease duration (months)		27±8.88 <sup>a</sup>	60±26.29	91.86±58.03 <sup>a</sup>	36 (12–156)	0.002*
		p=0.004*		p=0.330		
DAS 28		2.58 (1.98–5.49)	4.05 (2.58–5.49)	3.57±1.31	3.7 (1.68–5.71)	0.591
		p=0.328		p=0.754		
RF	Positive	3	0	30 <sup>a</sup>	2 <sup>a</sup>	0.011*
		p=0.229		p=0.011*		
Anti-CCP	Positive	4	2	36	4	0.094
		p=1.000		p=0.024*		
Rheumatoid nodule	Positive	1	0	4	0	0.611
		p=1.000		p=0.580		
Methotrexate+glucocorticoid		0	1	4	0	0.394
Methotrexate+sulfasalazine		6	3	35	6	
Leflunomide		0	1	1	2	
Biologics		3	1	18	6	
		p=0.315		p=0.097		

Significance level \* $p < 0.05$ ; <sup>ab,cd,e</sup>: same letters in the same rows show where the significant differences found by comparing four groups with Kruskal-Wallis test; n: number of subjects; EORA: elderly-onset rheumatoid arthritis; YORA: young-onset rheumatoid arthritis; DAS 28: disease activity score 28; TMJ: temporomandibular joint; RF: rheumatoid factor; anti-CCP: anti-cyclic citrullinated peptide.

**Table 3.** Comparison of the patients with and without temporomandibular joint involvement according to magnetic resonance imaging findings.

	EORA		YORA		p-value
	TMJ involvement positive n=9	TMJ involvement negative n=6	TMJ involvement positive n=58	TMJ involvement negative n=14	
Erosion positive	9 <sup>ab</sup>	0 <sup>ac</sup>	52 <sup>cd</sup>	0 <sup>bd</sup>	<0.001*
	p<0.001*		p<0.001*		
Resorption of the condyle positive	7 <sup>abc</sup>	0 <sup>a</sup>	10 <sup>b</sup>	0 <sup>c</sup>	<0.001*
	p=0.007*		p=0.193		
Flattening of the condyle positive	6 <sup>a</sup>	0	28 <sup>b</sup>	0 <sup>ab</sup>	0.001*
	p=0.028*		p=0.001*		
Narrowing of the joint space positive	4	0	24 <sup>a</sup>	0 <sup>a</sup>	0.007*
	p=0.103		p=0.003*		
Joint effusion positive	1	0	18 <sup>a</sup>	0 <sup>a</sup>	0.030*
	p=1.000		p=0.015*		
Osteophytes positive	7 <sup>ab</sup>	0 <sup>ac</sup>	44 <sup>cd</sup>	0 <sup>bd</sup>	<0.001*
	p=0.007*		p<0.001*		
Disk perforation positive	0	0	8	0	0.226
	Not computed		p=0.341		

Significance level \*p<0.05; <sup>a,b,c,d</sup>: same letters in the same rows show where the significant differences found by comparing four groups with Kruskal-Wallis test; n: number of subjects; EORA: elderly-onset rheumatoid arthritis; YORA: young-onset rheumatoid arthritis.

EORA patients, this difference was not statistically significant. There was no difference between the groups in terms of disease activity in our study. It seems possible that there may be a difference in terms of TMJ involvement. TMJ involvement may be higher in patients with long disease duration. In addition, the tendency to progress more aggressively may be associated with the higher incidence of TMJ involvement.

There was no difference between those with and without TMJ involvement in the EORA group in terms of mean age, gender, DAS 28, RF positivity, anti-CCP positivity, extra-articular findings, or use of DMARDs. Only the disease duration of the patients with TMJ involvement was shorter, which we expected to be the opposite. These findings suggest that clinical and laboratory features do not differ so much in EORA patients with and without TMJ involvement.

Erosion, resorption, flattening of the condyle, and osteophytes were the most common MRI findings in the EORA patients with TMJ involvement. Erosion, flattening of the condyle, narrowing of the joint space, joint effusion, and osteophytes were the most common MRI findings in the YORA patients with TMJ involvement. There was no difference between EORA and YORA patients with TMJ involvement in terms of MRI findings.

In our study, the proportion of EORA was found to be higher (17.2%) than in the literature. In the literature, the

frequency of RA in the geriatric population is reported as 2–2.4%<sup>3,4</sup>. Our finding may be due to the fact that our study population was not reflecting the general population. TMJ disorders and complaints are reported to be more frequent in elderly population<sup>13</sup>, and only the patients with TMJ complaints who were referred to a dental clinic were included in this study. However, we should keep in mind that patients now have easier access to experienced rheumatologists and dentists dealing with TMJ involvement and/or the elderly population that has increased over the years, which indicates that the number of EORA patients increases.

In our study, the disease duration of the YORA patients was significantly higher than that of the EORA group. Also, the mean age of the YORA patients with TMJ involvement was higher than the patients without TMJ involvement. This may indicate that disease duration and advancing age can be counted among the determining factors in terms of TMJ involvement in young patients.

Female dominance of RA and its lower incidence in men indicate that there is a hormonal effect on this disease<sup>14</sup>. The incidence in men rose steeply with age, whereas the incidence in women fell in the very elderly. In our study, male/female ratio of EORA group was higher than that of the YORA group, but this difference was not significant. When we looked at the literature, we identified studies

showing the gender distribution of patients with EORA and YORA similar<sup>15-18</sup>.

Since being positive for anti-CCP and RF is an important prognostic factor, the variable findings of studies complicate to explain the different prognosis and clinical course seen in patients of different ages. In our study, RF positivity was numerically low in the EORA group, but this difference was not statistically significant. Also, in the YORA group, RF positivity and anti-CCP positivity were more frequent in patients with TMJ involvement. Similar to our finding, Calvo-Alen et al.<sup>16</sup> stated that the frequency of RF was similar in EORA and YORA patients. We know that RF increases with age. However, there are studies that found less RF positivity in EORA compared to YORA<sup>19</sup>. In our study, anti-CCP positivity was similar in both groups. Besides our study, in the studies of Cho et al.<sup>18</sup> and Krams et al.<sup>17</sup>, anti-CCP was evaluated. Contrary to our study, the anti-CCP was found to be lower in the elderly in these two studies.

In our study, we could not find a significant difference in the use of DMARDs. Similar to our study, Cho et al.<sup>18</sup> found no difference between EORA and YORA in terms of DMARD use, but they found steroid doses higher in YORA patients. Takeda et al.<sup>20</sup> claimed that low-dose use of methotrexate is more common in elderly patients. Contrary to our results, Calvo-Alen et al.<sup>16</sup> detected the use of DMARDs and the use of combined DMARDs less in EORA patients than in YORA patients. Here, the difference in the treatment regimens is due to the difference in the management of side effects and complications. The limitation of our study is that the doses and the preference for biologic therapy were neglected.

In our study, when we compared the mean DAS 28 score of EORA and YORA patients, we could not find a difference. There are different results in the literature in terms of disease activity in EORA and YORA. Some studies reported that the disease activity in EORA and YORA patients was found to be

similar, which is consistent with our study<sup>16,18</sup>. Contrary to our study, Krams et al.<sup>17</sup> found the median value of the Simplified Disease Activity Index to be higher in EORA patients than in YORA patients.

To the best of our knowledge, this is the first study to examine whether there was a difference between YORA and EORA according to TMJ involvement and MRI findings. One of the limitations of our study is that it was designed retrospectively. It will be possible to obtain more reliable results through prospective multicenter studies with long follow-up periods. Another limitation is the small number of patients included in the study, particularly in the EORA group.

## CONCLUSION

According to our findings, EORA is not much different from YORA in terms of TMJ involvement, MRI findings, and clinical and laboratory features, but we would like to emphasize the importance of evaluating TMJ involvement in each RA patient.

## ACKNOWLEDGMENTS

The authors thank Prof. Dr. Peruze Çelenk for her supervisory role.

## AUTHORS' CONTRIBUTIONS

**MI:** Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **II:** Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

## REFERENCES

- Ozer PK, Sahin O, Ozer Z, Cengiz AK, Durmaz Y, Kaptanoglu E. Ultrasound-defined remission for good functional status in rheumatoid arthritis. *Indian J Med Res.* 2017;146(2):230-6. [https://doi.org/10.4103/ijmr.IJMR\\_548\\_15](https://doi.org/10.4103/ijmr.IJMR_548_15)
- Venetsanopoulou AI, Kalpourtzis N, Alamanos Y, Gavana M, Vantarakis A, Hadjichristodoulou C, et al. Prevalence of rheumatoid arthritis in Greece: results from the national health examination survey EMENO. *Rheumatol Int.* 2023;43(7):1349-55. <https://doi.org/10.1007/s00296-023-05316-3>
- Rasch EK, Hirsch R, Paulose-Ram R, Hochberg MC. Prevalence of rheumatoid arthritis in persons 60 years of age and older in the United States: effect of different methods of case classification. *Arthritis Rheum.* 2003;48(4):917-26. <https://doi.org/10.1002/art.10897>
- Villa-Blanco JI, Calvo-Alén J. Elderly onset rheumatoid arthritis: differential diagnosis and choice of first-line and subsequent therapy. *Drugs Aging.* 2009;26(9):739-50. <https://doi.org/10.2165/11316740-000000000-00000>
- Zhang Q, Liu Q, Lin C, Baima Y, Li H, Gong H, et al. The prevalence of rheumatoid arthritis in middle-aged and elderly people living in Naqu City, Tibet, Autonomous Region of China. *J Orthop Surg Res.* 2020;15(1):338. <https://doi.org/10.1186/s13018-020-01883-4>
- Watanabe R, Kadoba K, Tamamoto A, Murata K, Murakami K, Onizawa H, et al. CD8<sup>+</sup> regulatory T cell deficiency in elderly-onset rheumatoid arthritis. *J Clin Med.* 2023;12(6):2342. <https://doi.org/10.3390/jcm12062342>

7. Ilhanli M, Ilhanli I, Durmaz Y, Cengiz AK, Celenk P. Awareness of temporomandibular joint involvement in rheumatoid arthritis patients by physicians dealing with rheumatology. *J Exp Clin Med.* 2022; 39(3):842-7.
8. Jalal RA, Ahmed KM, Saeed SM, Qaradaghi TA. Correlation of clinical findings of temporomandibular joint with serological results in rheumatoid arthritis patients. *Clin Exp Dent Res.* 2022;8(5):1270-6. <https://doi.org/10.1002/cre2.621>
9. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. Rheumatoid arthritis classification criteria: an American College of Rheumatology/European league against rheumatism collaborative initiative. *Arthritis Rheum.* 2010;62(9):2569-81. <https://doi.org/10.1002/art.27584>
10. Cordeiro PC, Guimaraes JP, Souza VA, Dias IM, Silva JN, Devito KL, et al. Temporomandibular joint involvement in rheumatoid arthritis patients: association between clinical and tomographic data. *Acta Odontol Latinoam.* 2016;29(3):123-9. PMID: 28383601
11. Hair JBW, Babin B, Anderson R, Tatham R. Multivariate data analysis. Essex: Pearson Education Limited; 2013.
12. Yadav S, Yang Y, Dutra EH, Robinson JL, Wadhwa S. Temporomandibular joint disorders in older adults. *J Am Geriatr Soc.* 2018;66(6):1213-7. <https://doi.org/10.1111/jgs.15354>
13. Valesan LF, Cas CD, Réus JC, Denardin ACS, Garanhani RR, Bonotto D, et al. Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. *Clin Oral Investig.* 2021;25(2):441-53. <https://doi.org/10.1007/s00784-020-03710-w>
14. Raine C, Giles I. What is the impact of sex hormones on the pathogenesis of rheumatoid arthritis?. *Front Med.* 2022;9:909879. <https://doi.org/10.3389/fmed.2022.909879>
15. Richter MD, Matteson EL, Davis JM, Achenbach SJ, Crowson CS. Comparison of biologic discontinuation in patients with elderly-onset versus younger-onset rheumatoid arthritis. *ACR Open Rheumatol.* 2019;1(10):627-31. <https://doi.org/10.1002/acr2.11083>
16. Calvo-Alén J, Corrales A, Sánchez-Andrada S, Fernández-Echevarría MA, Peña JL, Rodríguez-Valverde V. Outcome of late-onset rheumatoid arthritis. *Clin Rheumatol.* 2005;24(5):485-9. <https://doi.org/10.1007/s10067-004-1067-4>
17. Krams T, Ruyssen-Witrand A, Nigon D, Degboe Y, Tobon G, Fautrel B, et al. Effect of age at rheumatoid arthritis onset on clinical, radiographic, and functional outcomes: the ESPOIR cohort. *Joint Bone Spine.* 2016;83(5):511-5. <https://doi.org/10.1016/j.jbspin.2015.09.010>
18. Cho SK, Sung YK, Choi CB, Cha HS, Choe JY, Chung WT, et al. Do patients with elderly-onset rheumatoid arthritis have severe functional disability?. *Semin Arthritis Rheum.* 2012;42(1):23-31. <https://doi.org/10.1016/j.semarthrit.2012.02.004>
19. Turkcapar N, Demir O, Atli T, Kopuk M, Turgay M, Kinikli, G, et al., Late onset rheumatoid arthritis: clinical and laboratory comparisons with younger onset patients. *Arch Gerontol Geriatr.* 2006;42(2):225-31. <https://doi.org/10.1016/j.archger.2005.07.003>
20. Takeda T. Treatment strategy of elderly rheumatoid arthritis. *Nihon Rinsho Meneki Gakkai Kaishi.* 2016;39:497-504. <https://doi.org/10.2177/jsci.39.497>

