ISSN: 2469-5726

KABUL et al. J Rheum Dis Treat 2020, 6:079
DOI: 10.23937/2469-5726/1510079
Volume 6 | Issue 1
Open Access

Journal of
Rheumatic Diseases and Treatment

RESEARCH ARTICLE

The Relationship Between Disease Activity, Demographic and Characteristic Features in Individuals with Rheumatoid Arthritis

Elif GUR KABUL[1], Bilge BAŞAKCI ÇALIK[1], Ceren KORKMAZ[1], Ummuhan BAŞ ASLAN[1], Murat TASCI[2] and Veli COBANKARA[2]*

[1]School of Physical Therapy and Rehabilitation, Pamukkale University, Denizli, Turkey

[2]Department of Rheumatology, Medical Faculty of Pamukkale University, Denizli, Turkey

***Corresponding author:** *Bilge BASAKCI CALIK, Pamukkale University, School of Physical Therapy and Rehabilitation, Denizli, Turkey, Tel : 00-90-2582964278, Fax: 00-90-2582964494*

Abstract

Background: This study was planned to investigate the relationship between disease activity and demographic and characteristic features of a group of Turkish individuals with Rheumatoid Arthritis.

Methods: A total of 143 participants (120 females, 23 males, mean age = 50.32 ± 12.14 years) diagnosed with Rheumatoid Arthritis (RA) according to the American College of Rheumatology 2010 criteria, were included in the study. Demographic features (gender, body mass index) and disease-related characteristics features (duration of disease, morning stiffness, presence of deformity, presence of nodules, dry eye, nail abnormalities, Raynaud's phenomenon, osteoporosis, dyspnea at rest, exertional dyspnea) of the participants were recorded. Disease activity was calculated using Disease Activity Score 28 (DAS28). According to DAS28, the participants were divided into 3 groups as remission, low disease activity and moderate-high disease activity. Pearson Chi-square test was used to analyze the statistical difference between the disease activity and demographic and possible characteristics features of individuals with RA.

Results: In the analysis of the data, significant difference between remission and moderate-high disease activity was observed in morning stiffness, presence of deformity, presence of nodule, osteoporosis and exertional dyspnea; whereas statistically significant difference between low and moderate-high disease activity was observed in osteoporosis and dyspnea at rest ($p < 0.05$). In terms of demographic and characteristic features where the difference occurs, It was obtained that osteoporosis, exertional dyspnea, presence of nodüle, presence of deformity and morning stiffness poses a 1.97, 1.64, 1.62, 1.56 and 0.53-fold higher risk for moderate-high disease activity compared to the remission, respectively. It was obtained that osteoporosis and dyspnea at rest poses a 1.52 and 1.40--fold higher risk for moderate-high disease activity compared to the low disease activity, respectively.

Conclusion: It was observed that osteoporosis and dyspnea pose a risk for the active period of RA. According to these results, we think that the risk of developing dyspnea and decrease in bone quality in RA individuals in the active period is high due to inactivity. Therefore, we suggest that RA patients should be encouraged to continue their physical activities and increase their participation in the exercise to reduce their complaints of dyspnea and osteoporosis.

Keywords

Rheumatoid arthritis, Osteoporosis, Dyspnea, Disease, Risk

Objectives

Rheumatoid arthritis (RA) is the most common type of inflammatory arthritis causing pain and destruction, especially in peripheral joints [1]. Although it is a clinical picture characterized by symmetrical polyarticular pain and swelling, prolonged morning stiffness, weakness and fatigue, it shows in systemic involvements. These systemic involvements pose an important risk for the progression of the disease. Rheumatoid nodules, vasculitis, anemia, fatigue, weakness, weight loss, respiratory problems, lung and cardiac involvements may accompany [2-4].

In individuals with RA, symptoms such as pain, fatigue, decreased range of motion, joint damage, morning stiffness, decreased muscle mass, decreased muscle

Citation: KABUL EG, ÇALIK BB, KORKMAZ C, ASLAN UB, TASCI M, et al. (2020) The Relationship Between Disease Activity, Demographic and Characteristic Features in Individuals with Rheumatoid Arthritis. J Rheum Dis Treat 6:078. doi.org/10.23937/2469-5726/1510079

Accepted: February 29, 2020: **Published:** March 02, 2020

strength and endurance cause a decrease in physical activity and physical fitness levels [5].

Rheumatoid arthritis is also a chronic inflammatory disease that progresses with progressive joint deformity, causing osteoporosis and death, causing multiple organ damage [6,7].

Pulmonary manifestations is a very common condition in RA [8]. It has been reported that many drugs used in rheumatoid arthritis can also cause lung involvement [9].

RA can cause significant disability and functional limitations. It is also a great burden for the individual with RA, society and health system. In order to reduce the negative effects of RA on quality of life and socio-economic burden, it should be better understood in every respect. Therefore, there is a need for clinical information on risk factors, comorbidities, epidemiological data and complications. This information is necessary in determining the most appropriate management approach for individuals with RA [10-12]. In recent years, clinical and demographic characteristics features of individuals have been recorded in many countries for better understanding of RA [13-16].

The prevalence of RA in Turkey, according to a study made in 2006 is 0.36% [17]. It is known that RA shows various characteristics features according to the population affected by it. Most of the available information about RA was obtained from studies conducted in Europe and the United States [18,19]. There are very few studies on the Turkish population [20]. Therefore, information regarding demographic and clinical characteristics features of RA individuals in Turkey is not sufficient.

This study was planned and conducted to examine the relationship between disease activity and demographic and characteristic features of a group of Turkish individuals with RA.

Methods

Participants

A total of 143 participants (120 females, 23 males, mean age = 50.32 ± 12.14 years) diagnosed with Rheumatoid Arthritis (RA) according to the American College of Rheumatology 2016 criteria, were included in the study. The inclusion criteria were as follows: (a) Having RA diagnosis according to ACR 2016 criteria [21]. (b) Aged 18-65. (c) Being volunteer to participate in this study. The exclusion criteria were as follows: (a) Having other diseases affecting functions (orthopedic, neurological, cardiovascular and metabolic disease). (b) Comorbidity affecting upper extremity and hand functions (carpal tunnel syndrome, trigger finger, impingement syndrome, thoracic outlet syndrome, lateral and medial epicondylitis, hand osteoarthritis). (b) Cognitive impairments. (c) Pregnancy. (d) Illiteracy.

The ethics of the study was approved by local ethics committee. All individuals were informed verbally and informed consent forms were signed.

Outcome measures

The data were collected by the same rheumatologist and by the same physiotherapist in the same day face to face interview method in approximately 40 minutes.

Evaluations included disease activity and demographic features (gender, body mass index) and disease-related characteristics features (duration of disease, morning stiffness, presence of deformity, presence of nodules, dry eye, nail abnormalities, Raynaud's phenomenon, osteoporosis, dyspnea at rest, exertional dyspnea).

Disease Activity Score 28 (DAS28) was used to evaluate disease activity. This index is a combination of 28 swollen joints and 28 sensitive joints, assessment of patient's general medical condition and C reactive protein rate. Swollen and sensitive were assessed for 28 joints (0 = No and 1 = Yes). These 28 joints included 2 shoulder, 2 elbow, 2 wrist, 10 metacarpophalangeal joints, 2 interphalangeal thumbs, 8 proximal interphalangeal joints, and 2 knee joints. DAS28 indicates current condition of the patient in the clinic. A high score represents a high disease activity. (> 5.1 high disease activity; 3.2 < DAS28 ≤ 5.1 moderate disease activity; 2.6 < DAS28 ≤ 3.2 low disease activity; ≤ 2.6 remission) [22].

Participant were divided into 3 groups as "remission", "low disease activity" and "moderate-high disease activity" according to DAS 28.

Participants were divided into two groups as "normal" and "owerweight" according to BMI, as "early stage (≤ 2 years)" and "late stage (> 2 years)" according to duration of disease and as "≤ 60 sec" and " > 60 sec" according to morning stiffness.

The presence of deformity, presence of nodules, dry eyes, nail abnormalities, Raynaud's phenomenon, osteoporosis, dyspnea at rest, exertional dyspnea were recorded as "yes" or "no".

Statistical analysis

The data was analyzed by SPSS packet program. Continuous variables were given as mean ± standard deviation and categorical variables as numbers and percentages. Pearson Chi-square test was used to define the statistical difference between DAS28 and demographic and characteristic features. P value < 0.05 in the 95% confidence interval was considered as statistically significant.

Results

One hundred and forty-three participants (female = 120, male = 23) participating in the study; average age was 50.32 ± 12.15 years. Descriptive data of the demo-

graphic and disease-related characteristics features of the participants are shown in Table 1.

Descriptive data of the three groups in which the participants were separated according to DAS 28 and are shown in Table 2. Descriptive data of the groups formed according to the demographic and disease-related characteristics features of the participants and are shown in Table 3.

In the analysis of the data, significant difference between remission and moderate-high disease activity was observed in morning stiffness, presence of deformity, presence of nodule, osteoporosis and exertional dyspnea; whereas statistically significant difference between low and moderate-high disease activity was observed in osteoporosis and dyspnea at rest ($p < 0.05$). In terms of demographic and characteristic features where the difference occurs, It was obtained that osteoporosis, exertional dyspnea, presence of nodüle, presence of deformity and morning

Table 1: Descriptive data of the participants' demographic and disease related characteristics features.

Variables	Min.-Max.	X ± SD
Age (years)	20 - 65	50.32 ± 12.14
Body height (m)	1.34 - 1.78	1.61 ± 0.07
Body mass (kg)	45 - 170	72.98 ± 15.16
Body mass index (kg/m^2)	17.76 - 58.82	28.08 ± 5.72
Duration of disease (years)	0.04 - 30.00	7.98 ± 7.17
Morning stiffness (sec)	0.00 - 180.00	32.90 ± 44.38

Table 2: Distribution and descriptive data of the participants according to Disease Activity Score 28.

Disease Activity Score 28	n (%)	Min. - Max.	X ± SD
Remission	67 (46.9)	0.96 - 4.17	1.78 ± 0.53
Low disease activity	24 (16.8)	2.62 - 3.19	2.94 ± 0.19
Moderate-high disease activity	52 (36.5)	3.24 - 6.52	4.36 ± 0.93

Table 3: Descriptive data of the groups allocated according to the demographic and disease-related characteristics features of the participants.

	Total n (%)	Remission n (%)	Low DA n (%)	Moderate-High DA n (%)
Gender- Female	120 (83.9)	54 (80.6)	19 (79.2)	47 (90.4)
-Male	23 (16.1)	13 (19.4)	5 (20.8)	5 (9.6)
BMI - Normal	45 (31.5)	26 (38.8)	5 (20.8)	14 (26.9)
-Owerweight	98 (68.5)	41 (61.2)	19 (79.2)	38 (73.1)
Duration of disease (years) -Early stage (≤ 2 years)	41 (28.7)	18 (26.9)	6 (25.0)	17 (32.7)
-Late stage (> 2 years)	102 (71.3)	49 (73.1)	18 (75.0)	35 (67.3)
Morning stiffness (sec) -≤ 60 sec	124 (86.7)	63 (94.0)	20 (83.3)	41 (78.8)
> 60 sec	19 (13.3)	4 (6.0)	4 (16.7)	11 (21.2)
Presence of deformity -Yes	49 (34.3)	17 (25.4)	9 (37.5)	23 (44.2)
-No	94 (65.7)	50 (74.6)	15 (62.5)	29 (55.8)
Presence of nodules -Yes	24 (16.8)	8 (11.9)	2 (8.3)	14 (26.9)
-No	119 (83.2)	59 (88.1)	22 (91.7)	38 (73.1)
Dry eye -Yes	65 (45.5)	30 (44.8)	9 (37.5)	26 (50.0)
-No	78 (54.5)	37 (55.2)	15 (62.5)	26 (50.0)
Nail abnormalities -Yes	39 (27.3)	18 (26.9)	6 (25.0)	15 (28.8)
-No	104 (72.7)	49 (73.1)	18 (75.0)	37 (71.2)
Raynaud's phenomenon -Yes	30 (21.0)	9 (13.4)	7 (29.2)	14 (26.9)
-No	113 (79.0)	58 (86.6)	17 (70.8)	38 (73.1)
Osteoporosis -Yes	43 (30.1)	15 (22.4)	4 (16.7)	27 (51.9)
-No	97 (67.8)	52 (77.6)	20 (83.3)	25 (48.1)
Dyspnea at rest -Yes	28 (19.6)	11 (16.4)	2 (8.3)	15 (28.8)
-No	115 (80.4)	56 (83.6)	22 (91.7)	37 (71.2)
Exertional dyspnea -Yes	64 (44.8)	24 (35.8)	10 (41.7)	30 (57.7)
-No	79 (55.2)	43 (64.2)	14 (58.3)	22 (42.3)

DA: Disease activity.

Table 4: Investigation of risk factors associated with the demographic and disease-related characteristics features of RA individuals who are in the active period (low or moderate-high disease activity) according to DAS 28.

Variables	Remission and low disease activity		Remission and moderate-high disease activity		Low and moderate-high disease activity	
	OR (95% CI)	p*	OR (95% CI)	p*	OR (95% CI)	p*
Gender (Female/Male)	0.93 (0.40 - 2.16)	0.880	1.67 (0.77 - 3.63)	0.139	1.42 (0.75 - 2.69)	0.179
BMI (Normal/Owerweight)	0.50 (0.21 - 1.23)	0.111	0.72 (0.45 - 1.17)	0.173	1.10 (0.79 - 1.53)	0.569
Duration of disease (Early stage/late stage)	0.93 (0.41 - 2.06)	0.859	1.66 (0.76 - 1.78)	0.489	1.11 (0.82 - 1.52)	0.497
Morning stiffness (≤ 60 sec/> 60 sec)	0.48 (0.21 - 1.06)	0.112	**0.53** (0.36 - 0.79)	**0.013**	0.91 (0.64 - 1.30)	0.648
Presence of deformity (Yes/No)	1.50 (0.75 - 2.99)	0.259	**1.56** (1.05 - 2.32)	**0.031**	1.09 (0.80 - 1.47)	0.581
Presence of nodules (Yes/No)	0.73 (0.20 - 2.67)	0.628	**1.62** (1.08 - 2.42)	**0.037**	1.38 (1.05 - 1.80)	0.065
Dry eye (Yes/No)	0.80 (0.392 - 1.63)	0.537	1.12 (0.74 - 1.69)	0.571	1.17 (0.86 - 1.58)	0.310
Nail abnormalities (Yes/No)	0.93 (0.41 - 2.06)	0.859	1.05 (0.67 - 1.65)	0.811	1.06 (0.76 - 1.47)	0.727
Raynaud's phenomenon (Yes/No)	1.93 (0.96 - 3.86)	0.082	1.53 (1.02 - 2.31)	0.065	0.96 (0.68 - 1.37)	0.839
Osteoporosis (Yes/No)	0.80 (0.31 - 2.05)	0.634	**1.97** (1.32 - 2.94)	**0.001**	**1.55** (1.15 - 2.09)	**0.006**
Dyspnea at rest (Yes/No)	0.54 (0.14 - 2.04)	0.331	1.45 (0.95 - 2.19)	0.104	**1.40** (1.08 - 1.82)	**0.046**
Exertional dyspnea (Yes/No)	1.19 (0.60 - 2.39)	0.611	**1.64** (1.08 - 2.48)	**0.017**	1.22 (0.89 - 1.68)	0.193

OR: Odds Ratio, CI: Confidence Interval, *Pearson Chi-square test.

stiffness poses a 1.97, 1.64, 1.62, 1.56 and 0.53-fold higher risk for moderate-high disease activity compared to the remission, respectively. It was obtained that osteoporosis and dyspnea at rest poses a 1.52 and 1.40-fold higher risk for moderate-high disease activity compared to the low disease activity, respectively (Table 4).

Discussion

As a result of our study, although it was determined that the increase in disease activity in individuals with RA was affected in many ways, it was observed that it posed the most risk in terms of osteoporosis and dyspnea.

There are contradictory results in the literature regarding the possible effect of gender and sex-dependent variables on the phenotype, severity and prognosis of RA. While some studies have reported that the number of women in remission is lower than men compared to DAS28, which is the predictive factor for the prognosis of RA [23-25]; some studies have reported that the severity of clinical disease activity, structural damage and deformities were similar in both sexes and there was no statistically significant difference in radiographic results between genders in RA [26-29]. When we examined the effect of gender, we found that disease activity was not more severe in women and we think that gender is not a determining factor in the severe course of the disease.

When Albrecht, et al. (2016) evaluated the three major RA cohorts in terms of BMI, they reported that most of them were overweight [30]. Tembe, et al. (2008) also showed that these patients had marginal weight gain [31]. Although it was observed that our RA individuals had high BMI, it was determined that BMI had no effect on disease activity. It has been shown in the literature that increased BMI in RA has an effect on many morbidity. Comparing normal and overweigt RA patients, it was concluded that the rates of rheumatoid cachexia and osteopenia increased significantly in overweight patients [32]. High BMI with RA has been associated with worse scores in patients and has been reported to negatively affect treatment [33,34]. It has been reported that increased BMI in RA should be treated and the solution is not just to lose weight [35]. We think that better results can be obtained by doing diet programs and exercise applications together in controlling increased weight gain in individuals with RA.

Yazıcı, et al. reported that the duration of morning stiffness reflects functional limitations and increased pain scores [36]. While the duration of morning stiffness was found to be significantly associated with DAS28 in the study by Orange, et al. [37]; Boers, et al. reported a low correlation in their study [38]. In parallel with the literature, we have seen that the increase in disease activity in individuals with RA is effective on the duration of morning stiffness.

Although direct evidence is limited, there is evidence between disease activity, functional status, and radiographic damage, and persistent synovitis in the hands has been reported to be a parameter associated with erosive changes [39,40]. In their study with 62 RA patients, Karaçavuş, et al. found that patients with high DAS28 scores had more peripheral joint involvement (mean 11/8 joints) than the patients with low disease activity [41]. In our study, we have concluded that the presence of deformity in RA poses a risk for the active

period of the disease. In order to obtain this result, there is a need for further investigation on which of the parameters used in the calculation of DAS28 (the number of swollen joints and/or the number of sensitive joints and/or patient's general medical condition and/or CRP) is more effective.

From studies evaluating demographic and clinical characteristics in individuals with RA, Mota, et al. reported the presence of rheumatoid nodules 15.38% and Bal, et al. 3.2% [24,20]. Corbett, et al. and Mota, et al. have associated the increase in the incidence of rheumatoid nodules with the active period [24,42]. They reported that nodules were more common in severe RA and they tended to disappear with the regression of articular involvement [43]. While we determined the presence of nodules as 16.8% in our study, we obtained that the presence of nodules poses 1.62-fold higher risk for moderate-high disease activity compared to the remission, Bal, et al. declared eye involvement as 4.8% in their study examined demographic and clinical characteristics of patients with RA in Turkey; Mota, et al. noticed the symptoms of sikka as 13.84% [20,24]. We determined the dryness of the eyes as 45.5% in the sample group of our study.

The first case-controlled study to identify nail changes significantly related to the disease in RA was conducted by Michel, et al. In our study, we identified nail abnormalities as 27.3% in individuals with RA [44]. We believe that information on this subject is lacking in the literature and more research is needed.

RA is not frequently reported among the underlying causes of secondary Raynaud's phenomenon; however, some studies have shown that the Raynaud's phenomenon occurs much more in RA patients than thought [45]. Among the studies evaluating demographic and clinical characteristics features in individuals with RA, Mota, et al. found that 18.46% had a Raynaud's phenomenon; Saraux, et al. found that 54 of 332 RA individuals (17.2%) had a Raynaud's phenomenon [24,46]. When the patients with Raynaud's phenomenon are examined, it is revealed that the RA rate is between 5 and 7% [46]. We have found the presence of Raynaud's phenomenon in patients with RA at a high rate, such as 21.0%.

It has been reported that axial and appendicular bone loss starts from the first 6 months of RA. Clinical inflammation usually progresses with bone erosion, leading to functional limitations. Synovial osteoclastic formation results in bone erosion [47,48]. Osteoporosis is one of the major complications encountered in RA and there are studies reporting that individuals with RA have an increased risk of bone fracture in the literature [49-51]. According to the results of our study, osteoporosis is seen at 30.1% in RA. We obtained that the osteoporosis poses 1.97-fold higher risk for moderate-high disease activity compared to remission and poses 1.52-fold higher risk for moderate-high disease activity compared to low disease activity. It is known that the effect of physical activity is quite high in the prevention of osteoporosis [52]. The World Health Organization emphasizes that sufficient calcium and vitamin D, as well as strengthening exercises, are important for preventing osteoporosis [53]. It has been reported in the literature that exercise increases bone density, reduces the risk of fractures and significantly improves quality of life [54]. In addition to sunbathing and calcium supplementation, exercise is also recommended to prevent falls against osteoporosis, which is common in RA [55].

In a study by Doyle, et al. it was reported that 12% of individuls had hypoxia in lung involvement in RA [56]. People often avoid breathing-causing activities in order not to increase their symptom severity and maintain their current status. Fear of movement due to dyspnea leads to a decrease in physical activity levels and functional capacities, and not performing daily living activities. Zu Wallack and his colleagues defined the "dyspnoea-inactivity vicious circle" in their work [57]. In the systematic review conducted by Tierney, et al. It was found that physical activity level in RA patients was lower compared to healthy individuals [58]. According to the results of our study, dyspnea was the second parameter that posed the highest risk for the active period in RA.

Exercise therapy is recommended as a part of non-pharmacological treatment in rheumatic diseases [59]. In a review that examines the relationship between exercise and inflammation, exercise has been shown to produce anti-inflammatory responses, and positive adaptation to the muscles has been demonstrated if exercise is continued regularly [60,61]. It has been reported in the literature that exercise is effective in reducing the level of dyspnea and fatigue [62]. It has been shown that regular exercise increases aerobic capacity and physical fitness in RA patients [63,64]. In addition, exercise is recommended in RA treatment by being effective in coping with the disease [65,66].

Conclusion

In our study, it was observed that osteoporosis and dyspnea pose a high risk in the active period of RA. According to these results, we think that the risk of developing dyspnea and decrease in bone quality in RA individuals in the active period is high due to inactivity. Therefore, we suggest that RA patients should be encouraged to continue their physical activities and increase their participation in the exercise to reduce their complaints of dyspnea and osteoporosis. We also recommend that exercise be made a part of life and be done regularly.

Conflicts of Interest

The author reports no conflicts of interest in this work.

Author Contributions

EGK, UBA, and BBC designed the study. EGK and CK searched databases and performed the selection of studies; EGK and MT collected data; EGK and BBC analyzed the data; EGK, CK and BBC wrote the manuscript; UBA and VC contributed to writing and critically uprising the manuscript and approved the last version.

References

1. Mitchell DM, Spitz PW, Young DY, Bloch DA, McShane DJ, et al. (1986) Survival, prognosis, and causes of death in rheumatoid arthritis. Arthritis Rheum 29: 706-714.
2. Mac Donald R, Sorby K (2006) Protection and Preservation. In: L Ally, Maintaining occupational independence in clients with rheumatoid arthritis. Occupational Therapy Evidence in Practise for Physical Rehabilitation 101-128.
3. Hammond A, Jeffereson P (2005) Rheumatoid Arthritis. In: A Turner, M Foster, SE Jhonson, Occupational Therapy and Physical Dysfunction: Principles, Skills and Practise, 6: 543-565.
4. Hammond A (2004) What is the role of Occupational Therapist? Best Pract Res Clin Rheumatol 18: 491-505.
5. Conner TS, Tennen H, Zautra AJ, Affleck G, Armeli S, et al. (2006) Coping with rheumatoid arthritis pain in daily life: within–person analyses reveal hidden vulnerability for the formerly depressed. Pain 126: 198-209.
6. Grassi W, De Angelis R, Lamanna G, Cervini C (1998) The clinical features of rheumatoid arthritis. Eur J Radio 27: 18-24.
7. Goldring SR (2003) Pathogenesis of bone and cartilage destruction in rheumatoid arthritis. Rheumatol 42: 11-16.
8. Tanoue LT (1998) Pulmonary manifestations of rheumatoid arthritis. Clin Chest Med 19: 667-685.
9. Tanaka N, Kim JS, Newell JD, Brown KK, Cool CD, et al. (2004) Rheumatoid arthritis-related lung diseases: CT findings. Radiology 232: 81-91.
10. Boonen A, Severens JL (2011) The burden of illness of rheumatoid arthritis. Clin Rheumatol 30: S3-S8.
11. Filipovic I, Walker D, Forster F, Curry AS (2011) Quantifying the economic burden of productivity loss in rheumatoid arthritis. Rheumatology (Oxford) 50: 1083-1090.
12. Zhang W, Anis AH (2011) The economic burden of rheumatoid arthritis: beyond health care costs. Clin Rheumatol 30: S25-S32.
13. Kvien TK, Uhlig T (2003) The Oslo experience with arthritis registries. Clin Exp Rheumatol 21: S118-S122.
14. Lapadula G, Ferraccioli G, Ferri C, Punzi L, Trotta F, et al. (2011) GISEA: an Italian biological agents registry in rheumatology. Reumatismo 63: 155-164.
15. Sokka T (2005) Rheumatoid arthritis databases in Finland. Clin Exp Rheumatol 23: S201-S204.
16. Symmons DP, Silman AJ (2003) The Norfolk Arthritis Register (NOAR). Clin Exp Rheumatol 21: S94-S99.
17. Akkoc N, Akar S (2006) Epidemiology of rheumatoid arthritis in Turkey. Clin Rheumatol 25: 560-561.
18. Lee DM, Weinblatt ME (2001) Rheumatoid arthritis. Lancet 358: 903-911.
19. Callegari-Jacques SM, Grattapaglia D, Salzano FM, Salamoni SP, Crossetti SG, et al. (2003) Historical genetics: spatiotemporal analysis of the formation of the Brazilian population. Am J Hum Biol 15: 824-834.
20. Bal A, Ataman S, Bodur H, Rezvani A, Paker N, et al. (2015) Characteristics of Patients With Rheumatoid Arthritis in Turkey: Results From the Turkish League Against Rheumatism Rheumatoid Arthritis Registry. Arch Rheumatol 30: 16-22.
21. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg D, Häuser W, et al. (2016) 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum 46: 319-329.
22. Wells G, Becker JC, Teng J, Dougados M, Schiff M, et al. (2009) Validation of the 28 jointDisease Activity Score (DAS28) and European League Against Rheumatism response criteria based on C-reactive protein against disease progression in patients with rheumatoid arthritis and comparison with the DAS28 based on erythrocyte sedimentation rate. Ann Rheum Dis 68: 954-960.
23. Sokka T, Toloza S, Cutolo M, Kautiainen H, Makinen H, et al. (2009) Women, men, and rheumatoid arthritis: analyses of disease activity, disease characteristics, and treatments in the QUEST-RA study. Arthritis Res Ther 11: R7.
24. da Mota LM, Laurindo IM, dos Santos Neto LL (2010) Demographic and clinical characteristics of a cohort of patients with early rheumatoid arthritis. Rev Bras Reumatol 50: 235-248.
25. Mancarella L, Bobbio-Pallavicini F, Ceccarelli F, Falappone PC, Ferrante A, et al. (2007) Good clinical response, remission, and predictors of remission in rheumatoid arthritis patients treated with tumor necrosis factor-alpha blockers: the GISEA study. J Rheumatol 34: 1670-1673.
26. Pincus T, Sokka T, Kautiainen H (2005) Patients seen for standard rheumatoid arthritis care have significantly better articular, radiographic, laboratory, and functional status in 2000 than in 1985. Arthritis Rheum 52: 1009-1019.
27. Krishnan E, Fries JF (2003) Reduction in long-term functional disability in rheumatoid arthritis from 1977 to 1998: a longitudinal study of 3035 patients. Am J Med 115: 371-376.
28. Heiberg T, Finset A, Uhlig T, Kvien TK (2005) Seven year changes in health status and priorities for improvement of health in patients with rheumatoid arthritis. Ann Rheum Dis 64: 191-195.
29. Gossec L, Baro-Riba J, Bozonnat MC, Daurès JP, Sany J, et al. (2005) Influence of sex on disease severity in patients with rheumatoid arthritis. J Rheumatol 32: 1448-1451.
30. Albrecht K, Richter A, Callhoff J, Huscher D, Schett G, et al. (2016) Body mass index distribution in rheumatoid arthritis: collaborative analysis from three large German rheumatoid arthritis databases. Arthritis Res Ther 23: 149.
31. Tembe AG, Kharbanda P, Bhojani K, Joshi VR (2008) Profile of rheumatoid arthritis patients attending a private tertiary hospital rheumatology clinic. Indian J Rheumatol 3: 144-147.
32. Hugo M, Mehsen-Cetre N, Pierreisnard A, Pupier E, Cherifi B, et al. (2017) High body mass index in rheumatoid arthritis: why we should promote physical activity. Arthritis Res Ther 19: 2.

33. Gremese E, Carletto A, Padovan M, Atzeni F, Raffeiner B, et al. (2013) Obesity and reduction of the response rate to anti-tumor necrosis factor a in rheumatoid arthritis: an approach to a personalized medicine. Arthritis Care Res (Hoboken) 65: 94-100.

34. Ajeganova S, Andersson ML, Hafström I; BARFOT Study Group (2013) Association of obesity with worse disease severity in rheumatoid arthritis as well as with comorbidities: a long-term followup from disease onset. Arthritis Care Res (Hoboken) 65: 78-87.

35. Baker JF, Billig E, Michaud K, Ibrahim S, Caplan L, et al. (2015) Weight loss, the obesity paradox, and the risk of death in rheumatoid arthritis. Arthritis Rheumatol 67: 1711-1717.

36. Yazici Y, Pincus T, Kautiainen H, Sokka T (2004) Morning stiffness in patients with early rheumatoid arthritis is associated more strongly with functional disability than with joint swelling and erythrocyte sedimentation rate. J Rheumatol 31: 1723-1726.

37. Orange DE, Blachere NE, DiCarlo EF, Mirza S, Pannellini T, et al. (2019) Rheumatoid arthritis morning stiffness is associated with synovial fibrin and neutrophils. Arthritis Rheumatol 15.

38. Boers M, Buttgereit F, Saag K, Alten R, Grahn A, et al. (2015) What Is the Relationship Between Morning Symptoms and Measures of Disease Activity in Patients With Rheumatoid Arthritis? Arthritis Care Res (Hoboken) 67: 1202-1209.

39. Visser H, le Cessie S, Vos K, Breedveld FC, Hazes JM (2002) How to diagnose rhematoid arthritis early. A prediction model for persistent (erosive) arthritis. Arthritis Rheum 46: 357-365.

40. Désirée Van der Heijde (2003) Impact of imaging in established rhomatoid arthritis. Best Pract Res Clin Rheumatol 17: 783-790.

41. Karaçavuş S, Uçar M, Geçer FM, Balbaloğlu O, Nas Ö, et al. (2015) Bone scintigraphy, DAS 28 score and biochemical parameters in patients with Rheumatoid Arthritis. Journal of Harran University Medical Faculty 12: 2.

42. Corbett M, Dalton S, Young A, Silman A, Shipley M (1993) Factors predicting death, survival and functional outcome in a prospective study of early rheumatoid disease over fifteen years. Br J Rheumatol 32: 717-723.

43. Estel BAP, Massardo L, Wojdyla D (2008) Is there something we can learn from rheumatoid arthritis in Latin America? A descriptive report on an inception Cohort of 1093 patients [abstract]. Ann Rheum Dis 67: 336.

44. Michel C, Cribier B, Sibilia J, Kuntz JL, Grosshans E (1997) Nail abnormalities in rheumatoid arthritis. Br J Dermatol 137: 958-962.

45. Pallis M, Hopkinson N, Powell R (1991) Nailfold capillary density as a possible indicator of pulmonary capillary loss in systemic lupus erythematosus but not in mixed connective tissue disease. J Rheumatol 18: 1532-1536.

46. Saraux A, Allain J, Guedes C, Baron D, Youinou P, et al. (1996) Raynaud phenomenon in rheumatoid arthritis. Br J Rheumatol 35: 752-754.

47. Kelley WN, Harris ED, Ruddy S, Sledge CB (1997) Text book of rheumatology. Fifth edition. United States of America, WB Saunders Company 851-951.

48. Schett G (2006) Rheumatoid arthritis: inflammation and bone loss. Wien Med Wochenschr 156: 34-41.

49. Sinigaglia L, Varenna M, Girasole G, Bianchi G (2006) Epidemiology of Osteoporosis in Rheumatic Diseases. Rheum Dis Clin North Am 32: 631-658.

50. van Staa TP, Geusens P, Bijlsma JW, Leufkens HG, Cooper C (2006) Clinical assesment of the long term risk of fractures in patients with rheumatoid arthritis. Arthritis Rheum 54: 3104-3112.

51. Michel BA, Bloch DA, Wolfe F, Fries JF (1993) Fractures in rheumatoid arthritis: an evaluation of associated risk factors. J Rheumatol 20: 1666-1669.

52. Carter MI, Hinton PS (2014) Physical activity and bone health. Mo Med 111: 59-64.

53. World Health Organization (2010) Global recommendations on physical activity for health. Geneva: World Health Organization.

54. Pamuk G, Kutlu R, Çivi S (2014) Evaluation of Quality of Life in Postmenopausal Women with and without Osteoporosis using the QUALEFFO-41 Scale. Turk J Phys Med Rehab 60: 139-146.

55. Pereira IA, Mota LM, Cruz BA, Brenol CV, Fronza LS, et al. (2012) 2012 Brazilian Society of Rheumatology Consensus on the management of comorbidities in patients with rheumatoid arthritis. Rev Bras Reumatol 52: 474-495.

56. Doyle JJ, Eliasson AH, Argyros GJ, Dennis GJ, Finger DR, et al. (2000) Prevalence of pulmonary disorders in patients with newly diagnosed rheumatoid arthritis. Clin Rheumatol 19: 217-221.

57. ZuWallack R (2007) How are you doing? What are you doing? Differing perspectives in the assessment of individuals with COPD. Copd 4: 293-297.

58. Tierney M, Fraser A, Kennedy N (2012) Physical Activity in Rheumatoid Arthritis. A Systematic Review. J Phys Act Health 9: 1036-1048.

59. Braun J, van den Berg R, Baraliakos X, Boehm H, Burgos-Vargas R, et al. (2011) 2010 update of ASAS/EULAR recommendations for management of ankylosing spondylitis. Ann Rheum Dis 70: 896-904.

60. Louis E, Raue U, Yang Y, Jemiolo B, Trappe S (2007) Time course of proteolytic, cytokin, and myostatin gene expression after acute exercise in human skletal muscle. J Appl Physiol 103: 1744-1751.

61. Perandini LA, de Sá-Pinto AL, Roschel H, Benatti FB, Lima FR, et al. (2012) Exercise as a therapeutic tool to counteract inflammation and clinical symptoms in autoimmune rheumatic diseases. Autoimmun Rev 12: 218-224.

62. Sarıtaş S, Tan M (2016) Effects of Exercise on Dyspnea and Fatigue in Patients with Heart Failure. Turkiye Klinikleri J Intern Med Nurs-Special Topics 2: 30-36.

63. Van Den Ende CH, Vliet Vlieland TP, Munneke M, Hazes JM (2000) Dynamic exercise therapy for rheumatoid arthritis. Cochrane Database Syst Rev 2: CD000322.

64. Kettunen JA, Kujala UM (2004) Exercise therapy for people with rheumatoid arthritis and osteoarthritis. Scand J Med Sci Sports 14: 138-142.

65. Luqmani R, Hennell S, Estrach C, Birrell F, Bosworth A, et al. (2006) British Society for Rheumatology; British Health Professionals in Rheumatology Standards, Guidelines and Audit Working Group. British Society for Rheumatology and british health professionals in Rheumatology guideline for the management of rheumatoid arthritis (the first two years). Rheumatology (Oxford) 45: 1167-1169.

66. Forestier R, André-Vert J, Guillez P, Coudeyre E, Lefevre-Colau MM, et al. (2009) Non-drug treatment (excluding surgery) in rheumatoid arthritis: clinical practice guidelines. Joint Bone Spine 76: 691-698.