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Original Article

Follow-Up Results of Our Patients with Rheumatoid Arthritis

Romatoid Artritli Hastalarımızın Takip Sonuçları

Tuğba YALÇIN, Ajda BAL, Deniz DÜLGEROĞLU, Aytül ÇAKCI

Department of Physical Medicine and Rehabilitation, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

Objectives: The aims of this study were to evaluate demographic and clinical characteristics of the patients with rheumatoid arthritis (RA), to compare laboratory, clinical, radiographic, and functional parameters at baseline and the last visit and to demonstrate changes in the functional status and radiographic grading.

Patients and methods: The files of 441 patients with RA who were followed in our Rheumotology Outpatient Clinic between January 2003 - December 2009 were retrospectively analyzed. The demographic and clinical characteristics as well as follow-up parameters at baseline and the last visit were recorded. In laboratory investigations, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were established. Disease activity, functional level and radiographic grading were determined using Disease Activity Score involving 28 joints (DAS28), Health Assessment Questionnaire (HAQ) and Larsen Score with anterior-posterior hand X-rays, respectively.

Results: Significant improvements were found in DAS28 and HAQ levels at the last visit, compared to baseline ($p<0.001$), while no significant change was observed in Larsen scores ($p=0.484$). Significant improvements were also observed only in CRP values at the last visit, compared to baseline ($p<0.001$). DAS28 scores of the patients without extra-articular involvement with a good compliance were found to be lower than in the others at the last visit ($p=0.043$, $p<0.001$).

Conclusion: Our results indicate that disease-modifying antirheumatic drug (DMARD) treatment in combination with regular follow-up is of utmost importance for the suppression of the disease activity in RA patients. Patients should be educated on drugs, as those with good compliance showed a better disease activity level.

Key words: Disease activity; follow-up; rheumatoid arthritis.

Amaç: Bu çalışmada romatoid artrit (RA) hastalarının demografik ve klinik özelliklerinin belirlenmesi, başlangıç ve son vizit sırasındaki laboratuvar, klinik, radyografik ve fonksiyonel parametrelerinin karşılaştırılması, hastalık aktivitesi, fonksiyonel durum ve radyografik evredeki değişimlerin gösterilmesi amaçlandı.

Hastalar ve yöntemler: Romatoloji Takip Polikliniği'mizde Ocak 2003 - Aralık 2009 tarihleri arasında takip edilen 441 RA hastasının dosyası retrospektif olarak incelendi. Demografik ve klinik özellikleri ve başlangıç ve son vizitteki takip parametreleri kaydedildi. Laboratuvar incelemesinde eritrosit sedimentasyon hızı (ESR) ve C-reaktif protein (CRP) değerleri not edildi. Hastalık aktivitesi, fonksiyonel düzey ve radyografik evreleme sırasıyla; 28 eklemi içeren Hastalık Aktivite Skoru (DAS28), Sağlık Değerlendirme Anketi (SDA), ön-arka el radyografisinde Larsen skoru kullanılarak yapıldı.

Bulgular: Başlangıç ve son vizit karşılaştırıldığında, DAS28 ve SDA düzeylerinde anlamlı iyileşme saptanırken ($p<0.001$), Larsen skorlarında anlamlı değişiklik gözlenmedi ($p=0.484$). Ayrıca son vizite laboratuvar paremetrelerinden yalnızca CRP değerlerinde anlamlı düzelme gözlendi ($p<0.001$). Eklem dışı tutulumu olmayan ve ilaç uyumu iyi olan hastaların son vizitteki DAS28 skorları, diğerlerine göre düşük bulundu ($p=0.043$, $p<0.001$).

Sonuç: Bizim sonuçlarımız, RA hastalarında kombine hastalık modifiye edici antiromatizmal ilaç (DMARD) tedavisinin ve düzenli takibin hastalık aktivitesini baskılamak için çok önemli olduğunu gösterdi. İyi ilaç uyumu olan hastaların hastalık aktivite düzeyi daha iyi olduğu için, hastalar ilaçlar konusunda eğitilmelidir.

Anahtar sözcükler: Hastalık aktivitesi; takip; romatoid artrit.

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Correspondence: Deniz Dülgeroğlu, M.D. Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, 06110 Dışkapı, Ankara, Turkey. Tel: +90 312 - 596 29 93 e-mail: denizdulgeroglu@gmail.com

Rheumatoid arthritis (RA) is a chronic, inflammatory, systemic, autoimmune disease with an undefined etiology. The disease progress may show differentiation between patients. While some patients exhibit short-term oligoarticular involvement together with small joint damage, others demonstrate severe polyarticular involvement accompanied by a clear functional failure. Since it affects some organs as well as the musculoskeletal system, it would not be correct to classify RA as merely a joint disease. The aim in treating this disease is to reduce pain and inflammation, keep joint structure and functions, and control systemic involvement.[1]

Assessing results is often difficult in inflammatory diseases of the musculoskeletal system. Detecting potential problems during treatment and evaluating the results are only possible if patients are regularly checked and constantly monitored.[2]

The Tight Control for Rheumatoid Arthritis (TICORA) study compared RA patients who were followed up routinely versus those followed up more intensively and found better results for disease activity, radiographic progression, physical function, and quality of life in the patients with intensive follow-up at no additional cost.[3]

Haraoui[2] reported a high value on frequent evaluation of RA patients and also stated that intensive follow-up allowed for the evaluation of patient response to treatment and provided the ability to alter the treatment based on clinical changes.

The aims of this study were to retrospectively evaluate RA patients who were referred to our Rheumatic Diseases Follow-up Outpatient Clinic between 2003-2009, to determine their demographic and clinical characteristics, and to compare laboratory, clinical, radiographic, and functional parameters at first presentation and last visit, thus demonstrating any changes in disease activity, functional status, and radiographic grading.

PATIENTS AND METHODS

Rheumatoid arthritis patients who were admitted to our hospital's Rheumatic Diseases Follow-up Unit between January 2003 - December 2009 and followed up during that same time period were evaluated retrospectively for this study.

The files of 441 patients diagnosed with RA according to the 1987 American College of Rheumatology (ACR) Classification Criteria[4] were examined, and their demographic and clinical characteristics and follow-up parameters were recorded. Retrospective data was obtained from the patients' files from their first visit, whereas prospective data from patients' examinations was gathered from their last six months of visits to our facility. In addition, the patients were questioned about drug compliance, exercise habits, physiotherapy cure, and orthosis usage during routine patient checkups for six months in 2009, and their final radiographic evaluations were performed.

The following data was recorded: patients' age, gender, education level, disease duration (months), follow-up time (months), age of disease onset (years), duration of diagnosis (years), drug use information (drugs currently being used), extra-articular involvement, presence of comorbid diseases, and family history. Additionally, the rate of osteoporosis in the patients was investigated. Patients with T scores of -2.5 and under in bone mineral density (BMD) measurements were considered to have osteoporosis.

Drug compliance was investigated with the following two questions during the final patient check-ups: "Do you take your medication at the recommended hours?" and "Do you take the recommended doses of your medication?". A "No" reply to one of these questions was considered as drug noncompliance. Also, the underlying factors (side effects, multiple drug use, inefficacy, forgetfulness, misconceptions, and social factors) regarding the noncompliance were identified.

Twenty-eight joints were evaluated for tenderness and swelling during the initial admission and final check-ups of the RA patients. Rheumatoid nodules and deformities in the hands and legs were noted during musculoskeletal system examinations at the patients' last visit.

Morning stiffness duration, erythrocyte sedimentation rate (ESR) (mm/hour), C-reactive protein (CRP) (mg/L), and rheumatoid factor (RF) (values over 15 IU/ml were positive) levels were measured at initial admission and the last visit.

Bilateral anterior-posterior hand-wrist radiography of the patients taken during their initial admissions and final check-ups were used for radiographic evaluation purposes. The type of RA was recorded as erosive or cystic based on these radiographies. The degree of radiographic joint involvement was assessed using the modified version of the Larsen scoring system developed by Edmonds.[5]

Table 1. Demographic characteristics of patients with rheumatoid arthritis

	n	%	Mean±SD	Min.-max.
Age			54.0±12.3	18-88
Gender				
Male	87	19.7		
Female	354	80.3		

SD: Standard deviation; Min.: Minimum; Max.: Maximum.

Patient global assessment was made using a 0-100 mm visual analog scale (VAS), and the pain level was assessed using a Likert scale.

Disease activity was evaluated using the Disease Activity Score-28 (DAS28) and grouped according to the European League Against Rheumatism (EULAR) disease activity criteria.[6]

An RA-related functional disability level was determined using the Health Assessment Questionnaire (HAQ), which has been validated and found to be reliable for Turkish.[7]

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) for Windows version 11.5 software. The distribution of continuous variables was investigated using the Shapiro-Wilk test, whether they were distributed normally or not. Descriptive statistics for continuous variables were given as mean ± standard deviation or median (1st quartile-3rd quartile). For nominal variables number of cases and percentage was used. The Mann-Whitney U-test was employed to compare the means of groups for two independent samples, and the Kruskal-Wallis test was utilized for more than two independent samples. For continuous variables, the Wilcoxon signed rank test was used, and for nominal variables, the McNemar test was used to evaluate the initial and final data, whether a statistically significant change had occurred within the groups or not. An evaluation of the correlation between continuous variables was performed using Spearman's correlation test. Results of $p<0.05$ were accepted as significant.

RESULTS

The demographic and clinical characteristics of the patients are presented in Tables 1 and 2. It was found that 46.7% of patients had one or more comorbid disease, and 17.2% of the patients presented with osteoporosis (Table 3). The percentage of RA patients found to have one or more extra-articular involvement was 21.5%, and the most frequent type was pulmonary involvement (Table 4).

Seventy (29.53%) of the 237 cases who underwent final examinations had at least one deformity. The hand and leg deformities in the RA patients are given in Table 5.

Patients' medications, determined at their last follow-up visit, are provided in Table 6. The percentage of patients who underwent combination therapy was 92.7%, and 6.8% had monotherapy. A very small percentage (0.5%) took no drugs. Therefore, determining clinical scores in order to make a statistical comparison between patients who used disease-modifying antirheumatic drugs (DMARDs) and those who did not was impossible.

Non-medical treatments as recommended to the patients are shown in Table 7, and the drug compliance rate and reasons for noncompliance are given in

Table 2. Clinical characteristics of patients with rheumatoid arthritis

	n	%	Mean±SD	Min.-max.
Disease duration (year)			11.9±9.2	0.04-60.0
Age of disease onset (year)			42.2±13.3	6-82
Duration of follow-up (month)			26.7±17.8	2-65
Diagnostic delay (year)			3.1±5.5	0-39
Family history	81	18.4		
Type of rheumatoid arthritis				
Erosive	200	59.3		
Cystic	137	40.7		
Rheumatoid nodule	33	7.5		
Extra-articular involvement	95	21.5		
Comorbid disease	206	46.7		
Rheumatoid factor positivity	262	59.4		

SD: Standard deviation; Min.: Minimum; Max.: Maximum.

Table 3. Comorbid diseases for patients with rheumatoid arthritis

	n	%
Hypertension	140	67.9
Diabetes mellitus	54	26.2
Hypothyroidism	25	12.1
Hyperthyroidism	23	11.1
Chronic obstructive pulmonary disease	12	5.8
Hyperlipidemia	12	5.8
Congestive heart failure	8	3.8
Tuberculosis	5	2.4
Arrhythmia	1	0.5

Table 8. The side effects caused by DMARDs are provided in Table 9.

A comparison of clinical and laboratory characteristics of RA patients during their initial admission and final check-ups revealed a statistically meaningful improvement in morning stiffness duration, pain level, patient global assessment, number of swollen and tender joints, CRP value, and DAS28 and HAQ scores is shown in Table 10. There were no statistically meaningful changes in the ESR and Larsen scores (Table 11). Despite there being no statistical changes in the Larsen score, radiological damage progression was found in 29.3% of the cases, even with the Larsen score remaining constant in 59.5% of the cases.

Disease activities of the RA patients, measured during the initial admission and final checkups and classified according to the EULAR disease activity criteria as remission, mild, moderate, and high, are shown in Figure 1.

Correlation analysis between the HAQ value and the Larsen score as well as the number of tender and swollen joints is shown in Table 12.

Table 5. Deformities of patients with rheumatoid arthritis

	n	%
Hand deformity		
Swan-neck	19	27.1
Ulnar drift	18	25.7
Z-deformity	16	22.8
Boutonniere	13	18.5
Interosseous muscle atrophy	5	7.1
Foot deformity		
Hallux valgus	18	25.7
Pes planus	16	22.8
Mallet finger	4	5.7
Clawing toe	3	4.2
Cock-up	1	1.4

Table 4. Extra-articular involvement of patients with rheumatoid arthritis

	n	%
Pulmonary	54	56.8
Sjögren's syndrome	16	16.8
Eye	13	13.6
Hematological	11	11.5
Renal	8	8.4
Vasculitis	3	3.1
Skin	2	2.1
Cardiac	1	1.0
Lymph edema	1	1.0
Amyloidosis	1	1.0

Comparison of the final DAS28 score and extra-articular involvement along with drug compliance are provided in Table 13.

DISCUSSION

We retrospectively evaluated 441 RA patients who were followed up at our Rheumatic Diseases Follow-up Clinic. The patients' final examinations, disease activities, and functional status revealed statistically significant improvement compared with their initial states. Radiological damage did not progress, and the majority of patients had drug compliance. A meaningful correlation was found between the final HAQ levels and the Larsen scores when compared with the number of tender and swollen joint.

The purpose of RA therapy is to put the disease into remission within a short period of time and maintain it for an extended period, thus preventing the emergence of complications and freeing the patient for daily life activities. One of the early arthritis evaluation recommendations published by the EULAR in 2007 contains the number of sensitive and swollen joints,

Table 6. Medications of patients with rheumatoid arthritis

	n	%
Drugs		
None	2	0.5
Monotherapy	30	6.8
Combination therapy	409	92.7
Drugs		
NSAID	357	81.0
Sulfasalazine	303	68.7
Methotrexate	257	58.3
Hydroxychlorochine	122	27.7
Leflunomide	83	18.8
Corticosteroid	65	14.7

NSAID: Nonsteroidal Antiinflammatory Drugs.

Table 7. Non-medical treatments for patients with rheumatoid arthritis

	n	%
Physical therapy	86	19.5
Exercise	45	10.2
Orthosis	34	7.7

global evaluation of the patient and the doctor, follow-ups in one to three month intervals, requisition of X-rays every six to 12 months in order to determine structural damage, and the employment of a functional measurement instrument, such as the HAQ, in disease activity monitoring.[8]

The aim of the follow-ups is to be able to control disease activity, identify any drug side effects, see the deformities in the joints and take appropriate measures to help the patient deal with them, evaluate any accompanying psychological problems and provide counseling if needed, and increase the patients' compliance with the disease and the therapy.[2]

In our study, the female/male ratio was about 4/1. This ratio is in keeping with previous studies.[9,10]

Sany et al.[10] in their study with French RA patients found the average age of disease onset to be 44 years old, and our study had a similar age of 42.

The delay between the disease onset and diagnosis in RA is reported to be nine months on average.[11] We found this time to be longer. This data might suggest that patients referred with joint complaints should be examined with particular attention paid to the possibility of RA.

Erosions, which are the signs of structural damage in RA, occur during the initial two-year early period of the disease. Radiological erosion was found in 59.3% of the patients in our study. Another study showed that 75.2% of the patients had erosion.[12]

Our study found the rheumatoid nodule rate to be 7.5%. In another study conducted in our country, the nodule rate was again found to be 7.5%.[9] Carmona et al.[13] reported the nodule rate in Spanish patients to be 24.5%. This data possibly suggests that RA presents with fewer nodules in Turkey and that the disease presents differently in various geographical regions.

Our study found extra-articular involvement to be 21.5%, but we evaluated nodule presence as a result of extra-articular involvement, which can cause an increased extra-articular involvement rate. The study of Calgüneri et al.[14] similarly reported extra-articular involvement to be 38.4%. In order of frequency, they found rheumatoid nodules in 18.1% of the patients, secondary Sjögren's syndrome in 11.4%, pulmonary involvement in 4.8%, Livedo reticularis in 4.8%, Raynaud's phenomenon in 3%, carpal tunnel syndrome in 2.8%, vasculitis in 1.3%, amyloidosis in 1.1%, and Felty syndrome in 0.3%.[14] In our study, pulmonary involvement was found to be the most common type of involvement other than

Table 8. Status of drug treatment compliance of patients with rheumatoid arthritis

	n	%
Compliance	36	15.4
No	198	84.6
Yes		
Reasons for noncompliance		
Side effects	20	55.6
Amnesia	8	22.2
Inefficiency	5	13.9
Multiple drug treatments	4	11.1
Social factors	2	5.6

Table 9. Adverse affects of disease-modifying antirheumatic drugs

	n	%
Methotrexate		
Gastrointestinal	107	69.4
Hepatotoxicity	21	13.6
Pulmonary	10	6.4
Mucosal ulceration	10	6.4
Hematological	8	5.1
Pruritus	2	1.2
Sulfasalazine		
Gastrointestinal	18	36
Hepatotoxicity	9	18
Nephrotoxicity	8	16
Hematological	8	16
Pruritus	7	14
Leflunomide		
Hepatotoxicity	7	25.9
Pruritus	6	22.2
Gastrointestinal	5	18.5
Hematological	3	11.1
Nephrotoxicity	2	7.4
Pulmonary	2	7.4
High blood pressure	2	7.4
Mucosal ulceration	1	3.7
Hydroxychlorochine		
Retinal toxicity	15	83.3
Gastrointestinal	2	11.1
Pruritus	1	5.5

Table 10. Comparison of clinical and laboratory parameters at first and last visit

	First visit		Last visit		
	Median	1st quartile-3rd quartile	Median	(1st quartile-3rd quartile)	*p*
Duration of morning stiffness (hour)	0.5	0-1	0.1	0-0.5	<0.001
Pain (Likert, 0-5)	2	1-3	2	1-2	<0.001
Patient global assessment (VAS, 0-100 mm)	50	30-70	50	20-50	<0.001
Swollen joint	1	0-3	0	0-1	<0.001
Tender joint	6	2-13	2	0-6	<0.001
C-reactive protein (mg/dl)	8.5	3.6-20.1	6.4	3.2-13.4	<0.001
ESR (mm/h)	27	17-44	27	18-39	0.362
DAS28	4.75	3.78-5.58	3.78	2.76-4.54	<0.001
HAQ	0.87	0.5-1.4	0.5	0.2-1.0	<0.001
Larsen score	24	24-30	24	0-30	0.484

VAS: Visual analog scale; ESR: Erythrocyte sedimentation rate; DAS28: Disease Activity Score-28; HAQ: Health Assessment Questionnaire.

rheumatoid nodules. These were followed by the presence of secondary Sjögren's syndrome and eye and hematological involvements.

In our study, 29.5% of cases showed no hand or leg deformities. Baysal et al.[15] in their study, found the most common form of leg deformity to be pes planus, whereas we found the most common form to be hallux valgus. This data reveals the need for the use of an orthosis that prevents and corrects deformities in order to increase patient functionality.

Hypertension was the most frequently presented disease with our RA patients. It has been reported that the incidence of hypertension increases in RA patients compared with the general population. This is most likely triggered by inflammation.[16]

Rheumatoid factor was found to be positive in 60-80% of RA patients.[17] In the aforementioned study by Calgüneri et al.,[14] 68.3% of patients were found to be RF positive, whereas RF positivity was 72.2% in the multi-centered study of Bodur et al.[9] In our study, RF positivity was 59.4%, which is lower than in previous studies. The lower rate of RF positivity most probably comes from the calibration difference between laboratories.

Table 11. Correlations between the changes in the Larsen Score, DAS28, the first HAQ, and disease duration

	r	*p*
Changes in DAS28	-0.015	0.791
First HAQ	0.066	0.307
Disease duration	0.195	<0.001

DAS28: Disease Activity Score-28; HAQ: Health Assessment Questionnaire.

Therapeutic approaches to RA have undergone changes over time with a better understanding of the efficacies and side effects of available drugs and the introduction of new therapy agents. Combination therapy was preferred in the RA patients that we followed. The steroid usage rate in our cases was found to be lower than other studies.[9] Although there have been patients who used small-dose steroids for extended periods at our clinic, they are normally used as a "bridge therapy" until signs emerge of the efficacy of the DMARDs. Therefore, only a minority of our patients used steroids for extended periods.

Our study examined whether patients had drug compliance and also looked at the underlying causes for non-compliance. We found that 84.6% of the patients we were able to question had complaints about the dosage and administration period of the prescribed drugs. In a study by Tuncay et al.,[18] it was observed that 11.6% of 86 RA patients followed for one year were constantly noncompliant. In our study, the higher number of patients might have increased the noncompliance rate. A study that explored the factors which underly drug noncompliance demonstrated that patients neglected to take the drugs mostly due to their side effects. Forgetfulness was the second most common reason for noncompliance, with inefficacy being the third and multiple drug use being the fourth, The "termination of social security benefits" or "inability to afford medicines" were underlying socioeconomic factors for noncompliance. The study by Tuncay et al.[18] also found that forgetfulness was the most common cause of patient noncompliance, with the second reason being dyspeptic complaints. These results show that forgetfulness is the most important

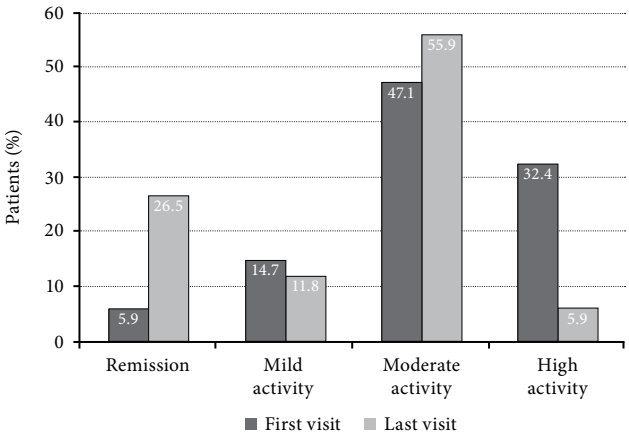

Figure 1. Activity levels of rheumatoid arthritis patients at first and last visit. DAS28 ≤2.6; Remission >2.6-≤3.2; Mild disease activity >3.2-≤5.1; Moderate disease activity >5.1 High disease activity.

factor in drug noncompliance in RA patients. Devising charts to remind the patients to take their drugs or having family member support could provide solutions to this problem.

We also determined the number of patients in our study who experienced drug side effects and the types of side effects that afflicted them. More patients (34.9%) were found to experience side effects due to methotrexate (MTX) usage. Gastrointestinal (GIS) and hepatic side effects are most frequently encountered in MTX therapy.[19] In our study, GIS side effects were found to be the most frequent, depending on MTX usage, and this was in agreement with the literature. The next most common side effects were hepatotoxicity, pulmonary involvement, mucosal ulceration, hematological side effects, and pruritus. As a result, the MTX therapy in 37.6% of the patients was discontinued, folic acid was added to the therapy in 46.1% of patients, and the subcutaneous MTX form was introduced in 9.7% of the patients for cases of gastrointestinal tolerance. Numerous studies, including a meta-analysis, exposed that folic acid and folinic acid reduced nausea and mucous membrane ulcerations, which are the primary side effects of MTX.[20] Administration of folic acid with MTX therapy in RA patients, started from the onset of the disease, could prove to be effective in reducing GIS side effects. Another alternative is the introduction of the subcutaneous form of MTX.

Table 12. Correlation between the last HAQ score and the last Larsen score along with an account of swollen and tender joints

	r	*p*
Larsen score	0.129	0.046
Swollen joint	0.239	<0.001
Tender joint	0.598	<0.001

HAQ: Health Assessment Questionnaire.

In a study which focused on a five-year follow-up of 102 RA patients receiving sulfasalazine (SSZ) therapy, the side effect rate was found to be 25.4%, with the most common side effects being GIS in nature.[21] In our study, side effects were found with SSZ usage in 16.5% of patients, with those associated with GIS issues being the most frequent. This type of therapy was discontinued in 84% of cases observed with side effects, and the dosage was reduced in the others.

The rate of side effects for leflunomide (LEF) was 6.3%. A study conducted in our country reported that LEF was discontinued due to hematological side effects and hepatotoxicity.[22] In our study, hepatotoxicity was found to be the most common side effect connected with LEF usage, followed by pruritus and GIS side effects.

The most severe side effect observed with hydroxychlorochine (HCQ) is retinal toxicity, which can result in loss of sight. Therefore, it should be emphazed that patients with RA need to be examined by an ophthalmologist prior to starting an anti-malarial therapy, and there should be subsequent routine checks.[23] In our study, we found that 4% of the patients showed side effects with HCQ, 83.3% of which were retinal toxicity. In these cases, HCQ therapy was discontinued.

We also identified non-medical therapy practices which had been recommended to the patients. A study by Vliet Vlieland[24] showed strong evidence for the efficacy of exercise and less evidence for joint protection programs, orthosis usage, and electrophysical modalities. Our study found that 19.5% of the patients received a minimum of one type of physical therapy throughout their disease period. The rate of exercising patients remained as low as 10.2%. The reason for the this might be lower education levels. When diagnosed, patients should be briefed and encouraged to exercise. The influence of non-medical therapy practices need not be ignored as they provide another link in the chain to aid the patients. We found that 8.4% of the patients were using orthosis, with the most common being insoles for pes planus and hand-wrist splints for carpal tunnel syndrome and ulnar drift.

Many studies have emphasized the importance of regular evaluation, and it has been suggested that such

Table 13. Correlation between the DAS28 score and extra-articular involvement and drug treatment compliance

	DAS28		
	Median	1st quartile-3rd quartile	*p*
Extra-articular involvement			
No	3.62	2.72-4.47	0.043
Yes	3.95	2.91-4.81	0.043
Drug treatment compliance			
No	4.62	3.34-5.39	<0.001
Yes	3.47	2.71-4.29	<0.001

DAS28: Disease Activity Score-28.

an intensive follow-up allows for better evaluation of the patients' response to therapy and improved results in disease activity, radiographic progression, physical function, and quality of life.[2,3] To follow up our RA patients, we have been using morning stiffness duration, number of sensitive and swollen joints, global assessments of the patient and the doctor, and pain level along with ESR and CRP values in order to monitor disease activity. In this study, a meaningful improvement was observed in morning stiffness duration, pain level, patient global assessment, and the number of sensitive and swollen joints in the patients' final follow-ups.

In the TICORA study, 55 RA patients were intensively followed up while 55 others were followed up in a routine fashion. They were monitored and compared for a period of 18 months. As a result, an improvement was found in sensitive joint, swollen joint, pain level, ESR, and CRP as well as in patient and doctor global assessments in both groups, with the ratio being higher in the patients followed more intensively.[3]

In the Computer Assisted Management in Early Rheumatoid Arthritis (CAMERA) study, 299 RA patients were followed up for a period of four years. The patients were classified into two groups: patients under a one-month interval intensive follow-up with a computer-controlled system and patients under a classical quarterly routine follow-up. Both groups were treated with the same dosage of MTX. Two years later, 50% of the intensively followed patients and 37% of the classically followed patients had been in remission for at least six months. Sensitive joint, swollen joint, ESR, and pain levels of both groups generally showed an improvement.[25]

In the TICORA and CAMERA studies,[3,25] a meaningful improvement was detected in the ESR and CRP levels as well as for acute-phase reactants, but in our study, only the CRP level showed significant improvement. As ESR is dependent upon plasma fibrinogen levels, it rises and improves later than CRP. As CRP's half-life is short, it is quickly restored to its normal value once the inflammation is over.[26] These results reinforce the view that the CRP level is more valuable for inflammation follow-ups.

Our study struggled to produce answers to the following questions: "How well did we treat the patients?" and "What is our disease activity score and remission rate at the end of the therapy?". A meaningful improvement was discovered in DAS28 scores compared with the scores at the onset of follow-up. When we grouped our results according to the EULAR disease activity criteria, it was found that the rate of patients with high disease activity was reduced in the final check-up compared with the initial admission, that the rate of patients in moderate disease activity remained nearly the same, and that the patient rates in mild disease activity and remission significantly increased. These findings demonstrated that a large portion of the patients benefited from therapy and follow-up, but some of them still needed additional therapy. Even in early-stage RA, remission rates do not go beyond 50-60% in the best series. Besides, there is limited data on the sustainability of remission.[27] Future goals include finding the best therapy for all patients and finding a cure for the disease.

Our study found disease activity was lower in the group with drug compliance. The high number of patients and extended monitoring period in our study also need consideration. This data might suggest drug compliance is important in controlling disease activity in RA; therefore, the patients need to be informed of this in order to increase their participation in therapy.

In a study by Nyhäll-Wåhlin et al.,[28] it was demonstrated that the risk of extra-articular involvement was higher during the two-year follow-up after diagnosis with RA in patients with high disease activity and disability and that these patients had worse prognoses. Likewise, our findings showed that disease activity was lower in the group with no extra-articular involvement, thus extra-articular involvement should be considered in patients with high disease activity.

The patients' functional levels as well as their disease activity levels need to be evaluated. The HAQ score is the most important functional indicator in determining "restrictedness", loss of labor, and mortality in advance. Therefore, it is one of the factors affecting prognosis in early-stage RA.[29] In the Combination Therapy in Early Rheumatoid Arthritis (COBRA) study and the Finnish Rheumatoid Combination Therapy (FIN-RACo) trial study, it was demonstrated that there were lower functional losses in five-year follow-ups, depending on the combination therapy.[30,31] Our data also found a meaningful improvement in the patients' functional disabilities after comparison of their HAQ scores during their initial admission and final check-ups. Another study followed 191 RA patients for five years, and the number of sensitive joints, pain level, disease activity level, and radiological progression along with ESR and CRP levels were found to be the predictive factors on the HAQ score.[32] In a study by Başkan et al.[33] it was found that there was a relationship between the HAQ and disease time, pain level, number of sensitive joints, Ritchie articular index (RAI), and laboratory parameters (ESR, CRP) in female patients, whereas male patients showed no relationship between the HAQ and disease time and laboratory parameters. There was only a relationship with the Larsen scores. In our study, a meaningful correlation was also found between the final check-up HAQ score and a combination of the final Larsen score and the number of sensitive and swollen joints. These results may indicate that functional levels were most affected by the number of sensitive and swollen joints.

In our study, the Larsen score was used to evaluate radiological damage. No meaningful difference was found in the increase between the change in our cases at onset and the final Larsen scores. Radiological progression was discontinued in 59.5% of our patients, and radiological damage progressed in 29.3%. While Kremer and Lee[34] argued that long-term therapy with MTX inhibits the radiographic progression of RA, Pullar et al.[35] reported that SSZ significantly reduced joint destruction. However, Uğur et al.[36] demonstrated in their cohort that radiological progression continued after a one-year follow-up period and that joint damage also continued to increase in patients who stayed in remission.

Li et al.[37] found a meaningful relationship between disease time and the Larsen score. In another study, a weak correlation was revealed between the HAQ score and the Larsen score, whereas in a study done in our country, the Larsen score was related to disease duration in female patients and the HAQ in male patients.[33,38] However, in our study, we found that the progression in the Larsen score increased parallel to an extension in disease duration and found no correlation between the change in the Larsen score and the functional level at onset and change in disease activity. In light of this data, despite today's RA therapy approaches, it is possible to conclude that radiological progression is still inevitable in patients who are in the advanced stages of the disease.

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