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Original article

Differences in the management of early and established rheumatoid arthritis

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ABSTRACT

Objective: To assess the differences in the clinical and therapeutic management of early and established rheumatoid arthritis (RA) in clinical practice.
Methods: Retrospective and multicentre study including 360 patients diagnosed with RA. During the 12 months prior to the study, onset, sociodemographic, clinical and therapeutic data were collected by clinical chart review.
Results: A total of 152 patients with early RA and 208 with established RA were studied. 97.5% had received disease-modifying anti-rheumatic drugs (DMARDs) and 43.6% a TNFa blocker between the diagnosis and the start of the study. Established RA patients used TNFa blockers more frequently than early RA patients (60.1% vs 21.1%, *P*<.001). Methotrexate was the most commonly used drug (70.6%). A treatment change was seen in 79% of patients with early RA and 60.6% of those with established RA. A dose change was the most frequent modification and an inadequate response the most frequent reason. A 25.8% of treatments were stopped due to adverse events. The mean (SD) decrease on DAS28 score was 0.9 (1.5) on early RA and 0.2 (1.0) on established RA patients. A 35.8% of early RA patients showed a good EULAR response, while only 16.2% among established RA patients (*P*<.001). Rheumatoid factor and radiological progression assessment were the most requested determinations in early RA (*P*<.05).
Conclusions: Spanish rheumatologists used biological drugs with a higher frequency in patients with more advanced disease, as recommended in the main clinical practice guidelines.
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Diferencias en el manejo de la artritis reumatoide precoz y establecida

Palabras clave:
Artritis reumatoide
Artritis precoz
Monitorización clínica
Antagonistas del TNF
Fármacos antirreumáticos

RESUMEN

Objetivo: Evaluar las diferencias en el manejo clínico y terapéutico de la artritis reumatoide (AR) precoz y establecida en la práctica clínica.
Pacientes y método: Estudio retrospectivo y multicéntrico en el que se incluyó a 360 pacientes con diagnóstico de AR. Mediante la revisión de historias clínicas se recogieron variables sociodemográficas, clínicas y terapéuticas en los 12 meses previos al inicio del estudio.
Resultados: Se estudió a 152 pacientes con AR precoz (ARp) y 208 con AR establecida (ARe). El 97,5% había recibido fármacos modificadores de enfermedad (FAME) y el 43,6% tratamiento anti-factor de necrosis tumoral (TNF) entre el diagnóstico y el inicio del estudio. Los anti-TNF fueron utilizados con mayor frecuencia en pacientes con ARe (el 60,1 frente al 21,1%; p < 0,001). El metotrexato fue el fármaco más

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utilizado (70,6%). Se detectó cambio del tratamiento en un 79% de pacientes con ARp y en el 60,6% con ARe. El cambio de dosis fue la modificación más frecuente y una respuesta inadecuada el motivo más frecuente. El 25,8% de los tratamientos se suspendieron por reacciones adversas. La disminución media ± desviación estándar del DAS28 fue 0,9 ± 1,5 en ARp y 0,2 ± 1,0 en ARe. El 35,8% de las ARp presentó buena respuesta EULAR, mientras sólo el 16,2% de las ARe (p < 0,001). La determinación del factor reumatoide y la valoración de la progresión radiológica fueron más solicitadas en la ARp (p < 0,05).
Conclusiones: Los reumatólogos españoles utilizaron agentes biológicos con mayor frecuencia en los pacientes con enfermedad más evolucionada, ajustándose a las recomendaciones de las principales guías de práctica clínica.

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Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease. Its chronic and progressive character creates a great impact on the patient's quality of life, which comes from functional disability and a decrease in life expectancy.[1] Its prevalence in Spain in the population over 20 years old is 0.5%.[2] Women are affected more by RA than men (3:1) and it appears more frequently between the ages of 40 to 60.[3] Its socio-economic repercussions are very great. The cost of RA in Spain in 2001 reached 2,250 million euros. Of this figure, 70% was due to direct costs and 30% to indirect costs.[4] The intangible costs, a consequence of deterioration in these patients' quality of life and its consequent family and social repercussions are more difficult to quantify. It is calculated that 5% of sick leave in our country is due to RA.[4-6]

Current therapeutic aims are based on symptomatic treatment of pain and inflammation, together with a background treatment that can alter the progress, delay structural damage and improve quality of life in a patient with RA.[7,8] The majority of guides and agreements recommend starting treatment with disease-modifying anti-rheumatic drugs (DMARDs) as soon as diagnosis is established.[7,9,10] Even so, each centre can apply its own changes due to health care or management reasons. Sometimes it even seems that experience and handling adapted to the characteristics and the progress of each case could determine the patient approach.

Our study aim was to get to know the clinical and therapeutic management of RA in Spain (ARES study) at rheumatology surgeries during usual clinical practice. To do so, the treatments used, together with their modifications during the time difference of patients with early RA (ERA) and patients with established RA (EstRA), were assessed.

Patients and methods

An observational, retrospective, multi-centre study was carried out in routine clinical practice conditions, where the clinical histories (CH) of patients with RA were reviewed within a timeframe of 1 year (12 months prior to each patient's inclusion date). The CH review of the ARES study was carried out during the first semester of 2007.

The CHs chosen corresponded to patients with RA selected through consecutive recruitment among patients of both sexes, who were over 18 years old and who visited a rheumatology surgery. Each researcher had to include 4 patients who had ERA and another 4 who had EstRA. The definition of ERA was a form of rheumatoid arthritis with an evolution time of ≤ 2 years and that of EstRA was those with > 2 years. All patients included signed a consent form to participate in the study before it started. The study had been previously approved by the reference bioethics committee and later by all the participating centres.

The following sociodemographic variables and clinical baselines were recorded: gender, age, family history of rheumatic disease, date of the start of RA symptoms and diagnosis, and history of disease-related surgical interventions. Data reported by the rheumatologist in the related visits during the year prior to the inclusion date of this study were also collected: attendance (number of visits), RA evolution and clinical-therapeutic management of the disease.

All the treatments used to control RA during the year prior to the inclusion were also recorded, as well as the treatment during the last visit of the period studied. The background treatments were grouped by therapeutic family and active principle to code them into three groups: DMARDs, agents neutralizing tumour necrosis factor (TNF antagonists or anti-TNF) and others.

All treatments received during the evolution of the disease were analysed, those of the previous year and those received during the last visit. The time elapsed until treatment modification was also considered for this analysis, defining treatment modification as any change, either of regime or dose. The reasons for termination by therapeutic group were likewise collected. Substitution was defined as any change in the active principle for this analysis. A survival analysis using the Kaplan-Meier method was carried out to analyse the duration of each of the treatments.

All care and follow-up measures taken during the year, as well as RA progress based on the European League Against Rheumatism (EULAR) response, were analysed.[11] This evolution was assessed according to the treatment received by the patient during the last revision period visit.

Sample size was calculated to allow the assessment of clinical and therapeutic management of RA, with a proportion (p) of 0.50, a precision of 7% and a significance level of 0.05. The theoretic sample of patients was 196 for each group, that is, 392 patients in total. Statistical analysis was performed for the overall sample group in a stratified manner based on whether the diagnosis was ERA or EstRA. A descriptive analysis of the sociodemographic and clinical sample variables was carried out, and a comparative analysis of these between the two study groups, through ANOVA and Student t tests for the continuous variables and through a χ^2 test for the categorical variables. A value of $P<.05$ was considered significant in all the tests. The results were analysed using the statistical package SAS version 8.02 for Windows®.

Results

Sociodemographic and clinical characteristics of the sample

The final sample was made up from a total of 360 patients, of which 42.2% (152) presented ERA and 57.8% (208) EstRA. Table 1 shows the demographic and clinical baseline statistics of the sample, which is complete and stratified by RA types. The average evolution time of ERA was 1 year and 5 years for EstRA ($P<.001$). The time between start of the symptoms and diagnosis was also less in the ERA group ($P<.001$).

There were 16.1% of patients that presented a history of other rheumatic diseases. An interesting fact is that 9.2% of the total sample had a family history of RA; this percentage was greater in the

Table 1
Sociodemographic and clinical characteristics of the sample

	ERA	EstRA	Total	*P*
Gender	n (%)	n (%)	n (%)	.36
Male	34 (22.4)	55 (26.5)	89 (24.7)	
Female	118 (77.6)	152 (73.1)	270 (75.3)	
Total	152 (100)	208 (100)	360 (100)	
	Mean±SD	Mean±SD	Mean±SD	
Age, years	52.4 (15.8)	55.2 (13.8)	54.0 (14.7)	.08
	Median (P25-P75)	**Median (P25-P75)**	**Median (P25-P75)**	
RA evolution time, years	1 (0-1)	5 (3-11)	2 (1-6)	<.001
Time of onset of symptoms, years	1 (1-1)	6 (3.5-11.5)	2 (1-7)	<.001
Time between symptom onset and RA diagnosis, years	0.3 (0.2-0.5)	0.5 (0.3-1.0)	0.3 (0.2-0.8)	<.001
Family history	**n (%)**	**n (%)**	**n (%)**	.22
No history	121 (79.6)	181 (87.1)	302 (83.9)	
RA	18 (11.8)	15 (7.2)	33 (9.2)	
Osteoarthritis	6 (3.9)	4 (1.9)	10 (2.8)	
Osteoporosis	3 (2.0)	5 (2.4)	8 (2.2)	
Polyarthritis	1 (0.7)	1 (0.5)	2 (0.6)	
Lupus	1 (0.7)	2 (1.0)	3 (0.8)	
Sjögren's syndrome	0 (0.0)	3 (1.4)	3 (0.8)	
Other history	5 (3.3)	2 (1.0)	7 (1.9)	

ERA indicates early rheumatoid arthritis; EstRA, established rheumatoid arthritis; RA, rheumatoid arthritis; SD, standard deviation.
The data are presented as the number of patients (n) and percentages (%), and as mean or medians (25th percentile-75th percentile).

ERA group (11.8% against 7.2% in EstRA), although this result was not significant.

During evolution, 13.3% of patients required surgery or synoviorthesis. Considering the results by groups, 3.3% of ERA patients were submitted to surgery or synoviorthesis at some time, while it was 20.7% in the patients with EstRA (Figure 1). The differences observed between the surgically operated patients of both groups were significant (*P*<.001).

Therapeutic management of rheumatoid arthritis: types of treatment and changes in prescribing

All patients had at some time received some treatment to control RA. There was a percentage of 97.5% (351) of patients that had received treatment with DMARDs; 43.6% (157) had been treated with anti-TNFs and 91.1% (328) with other types of treatment. There were differences in the proportion of patients who followed treatment with TNF antagonists (*P*<.001) or with other treatments (*P*=.04) according to RA type (Figure 2).

Table 2 presents treatments followed during the year prior to the inclusion date. Among patients with ERA, the proportion that received more than one DMARD at the same time was 8% greater than in EstRA, while the percentage of patients treated with anti-TNF was 35.1% higher in the EstRA group (*P*<.001). The most commonly-used active principles (≥10%) were: methotrexate (70.6%), prednisone (33.3%), etanercept (30%), leflunomide (29.4%), deflazacort (28.3%), indomethacin (17.8%), diclofenac 13.6%) and adalimumab (10.0%). With regards to current treatment, 59.4% were being treated with

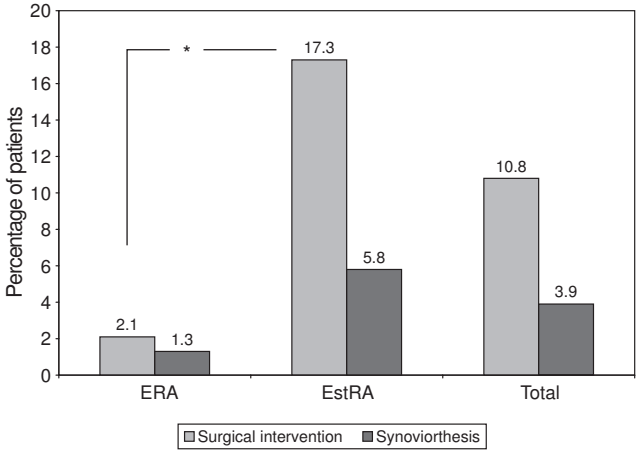

Figure 1. Patient distribution according to whether they had a history or not of surgery and/or synoviorthesis by RA type.
ERA indicates early rheumatoid arthritis; EstRA, established rheumatoid arthritis; RA, rheumatoid arthritis; SD: standard deviation.
The data are presented in percentage (%) of patients.
*Surgical intervention: *P*<.001 between both groups: ERA against EstRA.

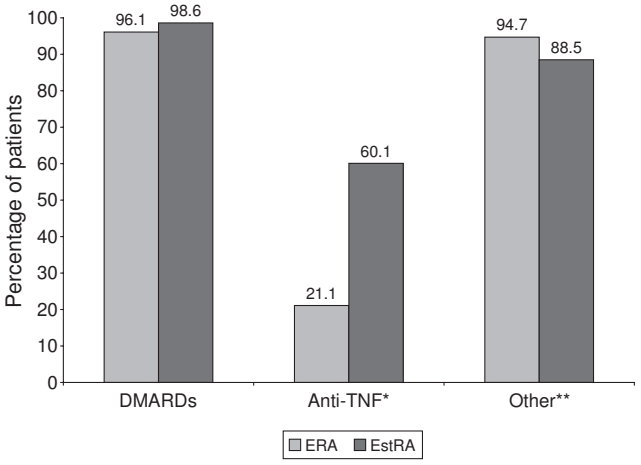

Figure 2. Distribution of background treatment for RA during disease evolution by RA type.
Anti-TNF indicates tumour necrosis factor antagonists; DMARDs, disease-modifying anti-rheumatic drugs; ERA, early rheumatoid arthritis; EstRA, established rheumatoid arthritis; RA, rheumatoid arthritis.
**P*<.001; ***P*=.04; ERA against EstRA.

Table 2
Treatment received during the last year and current treatment by RA type

	In the last year				Current treatment			
	ERA n (%)	EstRA n (%)	*P*	Total n (%)	ERA n (%)	EstRA n (%)	*P*	Total n (%)
Treatments received	151 (99.3)	207 (99.5)		358 (99.4)	147 (96.7)	205 (98.6)		352 (97.8)
DMARDs	143 (94.1)	166 (79.8)	.05	309 (85.8)	131 (86.2)	154 (74.0)	.005	285 (79.2)
1 DMARD	87 (60.8)	113 (68.1)	NS	200 (64.7)	101 (77.1)	131 (85.1)	NS	232 (81.4)
2 DMARDs	45 (31.5)	45 (27.1)	.08	90 (29.1)	24 (18.3)	19 (12.3)0.05	43 (15.1)	
3 DMARDs	8 (5.6)	7 (4.2)	NS	15 (4.8)	6 (4.6)	4 (2.6)	NS	10 (3.5)
> 3 DMARDs	3 (2.1)	1 (0.6)	NS	4 (1.3)	–	–	–	–
TNF antagonists	31 (20.4)	124 (59.6)	<.001	155 (43.1)	30 (19.7)	114 (54.8)	<.001	144 (40.0)
Others	139 (91.4)	176 (84.6)	.05	315 (87.5)	121 (79.6)	160 (76.9)	NS	281 (78.1)

DMARDs indicates disease-modifying anti-rheumatic drugs; ERA, early rheumatoid arthritis; EstRA, established rheumatoid arthritis; NS, not significant; RA, rheumatoid arthritis; TNF, tumour necrosis factor.
The data are presented as number of patients (n) and percentages (%).

methotrexate, 27.8% with etanercept, 25.8% with prednisone, deflazacort (23.1%), leflunomide (20.8%), indomethacin (14.2%) and diclofenac (11.7%); other active principles were used by less than 10% of patients.

There was a change in background treatment in 7 out of 10 patients, understanding this as any change in regime, dose or active principle (Table 3). This proportion was higher in patients with ERA with respect to those with EstRA (78.9 and 60.6%, respectively; *P*<.001). The most frequent type of change was the change of dose (36.4%) and the reason, a partial response or lack of response (46.7%).

The mean time elapsed between the start of treatment and the end of this due to withdrawal, substitution or change of active principle was in the case of DMARDs (2-3 years; confidence interval [CI] of 95%, 2.0-3.0) less than the TNF antagonists (3.6 years; 95% CI, 3.0-4.5) and to the rest of treatments (4.9 years; 95% CI, 3.7-8.7). The reasons for withdrawal were a lack of effectiveness, observed in 60.4% (464) of treatments; in 25.8% of cases (198), the treatment was stopped because of adverse reactions.

Attendance in following up rheumatoid arthritis

A total of 1,419 visits to the rheumatologist were recorded; 42.8% (607) corresponded to the ERA group and 57.2% (812) to the EstRA. Patients undertook 3-5 visits a year in 85.8% (309) of cases, which means a mean ± standard deviation (SD) of 3.9 ± visits/year, with no differences observed between the two groups. The main reason was the programmed disease control (Table 4). The determinants for erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) were the most requested tests and the 3-variable Disease Activity Score (DAS) and the Health Assessment Questionnaire (HAQ) questionnaire, the least requested. We must point out that the DAS28 was collected in 6 out of 10 visits and that differences between ERA and EstRA patients were appreciated only in determining rheumatoid factor and in assessing radiological progress; both tests were requested more often in patients with ERA (*P*<.05).

Evolution of rheumatoid arthritis clinical activity

Table 5 shows the evolution of disease activity according to RA type. We therefore see that patients with ERA show a mean decrease of ± SD in DAS28 values of 0.9±1.5 during the study against a variation of 0.2±1.0 in patients with EstRA (*P*<.001). The percentage of patients with a good EULAR response was greater in individuals with ERA (35.8%) compared to subjects with EstRA (16.2%) (*P*<.01). If we consider only patients with treatment with TNF antagonists, we also appreciate the differences between both groups in whether the improvement was excellent or good (*P*<.001).

Discussion

This study was designed to reflect the truth regarding clinical-therapeutic management of the patient with RA in rheumatology surgeries of our community. It had a considerable sample of patients

Table 3
Changes in background treatment for the disease during the follow-up year by RA type

	ERA n (%)	EstRA n (%)	Total n (%)	*P*
Receiving treatment changes	120 (78.9)	126 (60.6)	246 (68.3)	<.001
*Type of change**				
Change of drug	41 (27.0)	46 (22.1)	87 (24.1)	NS
Change of dosage	59 (38.8)	72 (34.6)	131 (36.4)	NS
Change of regime	10 (6.6)	26 (12.5)	36 (10.0)	.06
Other types of change	71 (46.7)	50 (24.0)	121 (33.6)	<.001
*Reasons for the change**				
Adverse reactions	21 (13.8)	31 (14.9)	52 (14.4)	NS
Partial response / no response	89 (58.6)	79 (38.0)	168 (46.7)	<.001
Other reasons	40 (26.3)	53 (25.5)	93 (25.8)	NS

ERA indicates early rheumatoid arthritis; EstRA, established rheumatoid arthritis; NS, not significant; RA, rheumatoid arthritis.
The data are presented as number of patients (n) and percentages (%).
*More than one change and more than one reason may be indicated.

Table 4
Attendance: reason for the visit and the proportion of patients with RA examinations in the last year

	ERA n (%)	EstRA n (%)	Total n (%)	*P*
*Reason for the visit**				
Programmed control	556 (91.6)	779 (95.9)	1,335 (94.1)	<.001
RA complications	10 (1.6)	9 (1.1)	19 (1.3)	NS
Treatment administration	10 (1.6)	38 (4.7)	48 (3.4)	.002
Other reasons	41 (6.8)	25 (3.1)	66 (4.7)	.001
*Tests carried out**				
ESR	141 (92.8)	201 (96.6)	342 (95.0)	NS
CRP	145 (95.4)	199 (95.7)	344 (95.6)	NS
Rheumatoid factor	129 (84.9)	156 (75.0)	285 (79.2)	.02
DAS28	98 (64.5)	130 (62.5)	228 (63.3)	NS
3-variable DAS	20 (13.2)	15 (7.2)	35 (9.7)	.06
Presence of rheumatoid nodules	114 (75.0)	150 (72.1)	264 (73.3)	NS
Radiographic progression rating	94 (61.8)	104 (50.0)	198 (55.0)	.03
HAQ Questionnaire	63 (41.4)	77 (37.0)	140 (38.9)	NS

CRP indicates C reactive protein; DAS, Disease Activity Score; ERA, early rheumatoid arthritis; ESR, erythrocyte sedimentation rate; EstRA, established rheumatoid arthritis; HAQ, Health Assessment Questionnaire; NS, not significant; RA, rheumatoid arthritis.
The data are presented as number of patients (n) and percentages (%).
*There could be more than one reason for the visit and had more that one additional test carried.

for this; a stratified analysis according to RA type, whether early or established, could even be performed.

With relation to the demographic characteristics of the sample, we have to point out that it presents general characteristics according to the epidemiological data collected in scientific literature.[2] However, it is surprising that the ERA patient subgroup should present a mean age similar to the overall group. The raised mean age observed in the early group makes us think that there is a certain delay in diagnosis or in referral to the specialist. The percentage of patients with RA having a family history of RA was high in our study. We must highlight the great percentage of ERA patients and family history with EstRA, which is why there is possibly a greater awareness in this aspect in ERA patient anamnesis.

Nearly all patients included had received some sort of treatment during the year considered and more than 95% were currently being treated. There were a greater proportion of patients with ERA in treatment with DMARDs with respect to those with EstRA. Currently, general opinions recommend starting treatment with DMARDs in the 3 months following diagnosis.[7,9] In this way, the greater use of DMARDs in ERA obtained in our series adapts itself to the recommendations established by the Spanish Rheumatology Society, according to which treatment with at least one conventional DMARD is necessary, preferably methotrexate, in monotherapy or combined therapy, with rapid dose escalation of up to 20 mg in 2-3 months, unless there are symptoms of intoxication.[7,9,10,12,13]

However, the efficacy of DMARDs on radiological progression continues to be very debated, partly due to the different techniques used to assess joint damage.[14] The problem of DMARD treatment duration has come up in different studies that show that suspension after remission is accompanied with an exacerbation of the disease.[15] The risk of toxicity, together with the low percentage of patients who achieve remission,[16] could partly explain the fact that after 5 years of treatment only 40% of patients treated with methotrexate continue taking the medication and the percentage is even lower with other DMARDs.

During the last few years, anti-TNFs have been shown to be effective in more than half of patients with RA where conventional treatment had previously failed and it has shown that they could even induce remission of the disease.[17,18] The fact that, in our study, treatment with anti-TNF is used more frequently in EstRA patients reflects the way rheumatologists in Spain manage the disease according to what is established in the main therapeutic guides. Our findings are

Table 5
Evolution of disease activity by RA type

	ERA	EstRA	Total	*P*
DAS28 difference (mean±SD)*	0.9±1.5	0,2±1,0	0,5±1,3	<.001
*DAS28 changes**, n (%)*				<.001
Nil improvement/ no improvement	36 (44.4)	77 (69.4)	113 (58.9)	
Moderate	16 (19.8)	16 (14.4)	32 (16.7)	
Good/Excellent	29 (35.8)	18 (16.2)	47 (24.5)	
Total	81 (100)	111 (100)	192 (100)	
*DAS28 changes in patients with anti-TNF**, n (%)*				<.001
Nil improvement/ no improvement	8 (44.4)	36 (80.0)	44 (69.8)	
Moderate	5 (27.7)	6 (13.3)	11 (17.5)	
Good/Excellent	5 (27.7)	3 (6.7)	8 (13.7)	
Total	18 (100)	45 (100)	63 (100)	

DAS indicates Disease Activity Score; ERA, early rheumatoid arthritis; EstRA, established rheumatoid arthritis; RA, rheumatoid arthritis; SD, standard deviation; TNF, tumour necrosis factor.
The data are presented as the number of patients (n) and percentages (%), and as ± standard deviation averages.
*Difference between the first DAS28 determination 12 months before the baseline visit and the following determination.
**According to EULAR criteria.[11]

similar to the data recently published in the CORRONA study.[19] In this cohort, approximately a third of patients with RA received anti-TNF treatment, 40% EstRA cases against 25% ERA[19]; while in our study these percentages were 55% and 20%, respectively. It is possible that total financing of these treatments in our health system also favours the greater use of these biological therapies.

However, Van der Heijde et al[20] demonstrated that the greatest structural damage is produced in the first two years from the onset of the symptoms. If we add to this that the patient with active RA presents a higher TNF concentration in the synovial fluid, we could justify the prescription of anti-TNF drugs in ERA patients and the setting up an intensive treatment as soon as possible.[21,22] The COMET study[23,24] shows the efficacy of anti-TNF treatment as first line drugs when combined with methotrexate, achieving remission percentages of 50% in patients with ERA in the first year. The BeSt study has also shown that is possible to maintain remission even once the biological treatment has been stopped.[25]

With regards to the frequency and changes in treatment, the ERA group presented a greater number of changes, which was probably motivated by a more demanding approach to achieve early clinical remission.

In relation to the number of patient visits carried out to follow up and control RA, these were more frequent in EstRA patients, which is in accordance with the currently established recommendations.[7,26,27] However, visits due to complications and other reasons were more frequent in ERA cases with respect to those for EstRA. The most requested determinations in this group of patients were ESR and CRP (in more than 90% of visits), followed by rheumatoid factor and the assessment of rheumatoid nodule presence.

There are many response criteria in RA that allow the assessment of the disease.[28] The EULAR criteria[11,20,29] define the response (good, moderate and absent) according to certain cut-off points for absolute values and relative changes in DAS. Patients with an improvement in ERA reach only 30.6%, while those with ERA exceed 50%. These differences could be explained by the relationship that exists between inflammation and disability in the early stages of the disease.

This study presented some limitations. Firstly, its retrospective design carried out through CH review. The researcher probably did not have all the information, so there could be registration bias. However, to minimise this type of bias, we opted for choosing CH patients who regularly went to the surgeries and complied with all the criteria established in the protocol. In this way, we had the patients' collaboration and the possibility of interviewing them to record the variables that were absent in the CH. Secondly, it would have been better if some of the variables could have been related to different types of treatment. However, given the size of our sample and the great variety of therapeutic possibilities, this would have generated numerous miniscule groups that would have made final analysis more difficult; that is the reason why we chose to create larger treatment groups that would allow a more general interpretation of the results. Another point is that the determination of anti-cyclic citrullinated peptides was not specifically recorded as they are not a marker that is systemically determined in the clinical practice of patients with RA. It would also have been interesting to have clinical remission data on patients to assess the attendance of each of the study cohorts, although this information was not systemically gathered during the study.

To summarise, we could conclude that Spanish rheumatologists adapt to the main clinical practice guide recommendations with regards to clinical-therapeutic management of RA patients. The distribution of treatments according to RA type reflects correct application of the treatment scale currently recommended.

Financing

This study was carried out with the sponsorship and support of Wyeth-Farma, S.A.

Conflict of interest

E. Marced is the medical manager for the rheumatology area of the Medical Department at Wyeth-Farma. The rest of the authors have no conflict of interest in relation to this study.

Annex 1. Addendum (list of centres participating in the study)

Hospital de Basurto; Hospital de Bellvitge; H. Central de Asturias; Hospital Central de la Defensa Gómez Ulla; Clínica Girona; Hospital Clínico Lozano Blesa; Hospital Comarcal Alt Penedés; Hospital Comarcal de Melilla; Hospital Donostia; Hospital de El Escorial; Hospital de Elda; Hospital de Figueras; Hospital de Fuenlabrada; Hospital de Galdakao; Hospital General de Castellón; Hospital General de Ciudad Real; Hospital General de la Palma; Hospital General de Vic; Centro Médico de Especialidades Grande Covián; Hospital Insular de Gran Canaria; Hospital de Jerez; Hospital La Fe; Hospital de Llerena/Hospital de Zafra; Hospital de la Marina Baixa; Hospital Marqués de Valdecilla; Hospital Meixoeiro; Hospital de la Merced de Osuna; Hospital Morales Meseguer; Hospital Nuestra Señora del Prado; Hospital Nuestra Señora de Sonsoles; Hospital Nuestra Señora de Valme; Hospital d' Ontinyent Xàtiva; Hospital de Palamós; Hospital POVISA; Hospital La Princesa; Hospital Provincial de Córdoba; Hospital Puerta del Mar; Hospital de la Ribera; Hospital de Sagunto; Hospital San Pedro de Alcántara; Hospital San Rafael; Hospital Santa María del Rosell; Hospital de Torrecárdenas; Hospital Vall d'Hebrón; Hospital Virgen de la Concha; Hospital Virgen de la Macarena; Hospital Virgen de la Salud; Hospital Virgen del Puerto; Hospital Virgen del Rocío.

References

1. Lozano JA. Artritis reumatoide (I). Etiopatogenia, sintomatología, diagnóstico y pronóstico [accessed 2010 Jun 8]. Available from: http://external.doyma.es/pdf/4/4v20n08a13018371pdf001.pdf.
2. Carmona L, Gabriel R, Ballina FJ, Laffon A, Grupo de Estudio EPISER. Proyecto EPISER 2000: prevalencia de enfermedades reumáticas en la población española. Metodología, resultados del reclutamiento y características de la población. Rev Esp Reumatol. 2001;28:18-25.
3. Carmona L, Villaverde V, Hernández C, Ballina J, Gabriel R, Laffon A, the EPISER Study Group. The prevalence of rheumatoid arthritis in the general population of Spain. Rheumatology (Oxford). 2002;41:88-95.
4. Lajas C, Abásolo L, Bellajdel B, Hernández-García C, Carmona L, Vargas E, et al. Costs and predictors of costs in rheumatoid arthritis: a prevalence-based study. Arthritis Rheum. 2003;49:64-70.
5. Reginster JY. The prevalence and burden of arthritis. Rheumatology (Oxford). 2002;41(Suppl 1):3-6.
6. Domínguez A. Costes asociados a la artritis reumatoide. Rev Esp Econ Salud. 2003;2:212-7.
7. Guía de Práctica Clínica para el Manejo de la Artritis Reumatoide (GUIPCAR) en España. Marzo de 2007 [accessed 2010 Jun 8]. Available from: http://www.ser.es/practicaClinica/GUIPCAR_2007/Metodologia/Menu1_MetodolMeto.php.
8. Schwartzman S, Fleischmann R, Morgan J. Do anti-TNF agents have equal efficacy in patients with rheumatoid arthritis? Arthritis Res Ther. 2004;6(Suppl 2):S3-11.
9. American College of Rheumatology subcommittee on rheumatoid arthritis guidelines. Guidelines for the management of rheumatoid arthritis. Arthritis Rheum. 2002;46:328-46.
10. Tornero Molina J, Sanmartí Sala R, Rodríguez Valverde V, Martín Mola E, Marenco de la Fuente JL, González Álvaro I, et al. Actualización del Documento de Consenso de la Sociedad Española de Reumatología sobre el uso de terapias biológicas en la artritis reumatoide. Reumatol Clin. 2010;6:23-36.
11. Van Gestel AM, Prevoo ML, Van't Hof MA, Van Rijswijk MH, Van de Putte LB, Van Riel PL. Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis. Comparison with the preliminary American College of Rheumatology and the World Health Organization/International League Against Rheumatism Criteria. Arthritis Rheum. 1996;39:34-40.
12. Guidance on the use of etanercept and infliximab for the treatment of rheumatoid arthritis. National Institute for Clinical Excellence. Technology appraisal guidance No. 36 [accessed 2010 Jun 8]. Available from: www.nice.org.uk.
13. Verstappen SM, Jacobs JW, Van der Veen MJ, Heurkens AH, Schenk Y, Ter Borg EJ, et al, on behalf of the Utrecht Rheumatoid Arthritis Cohort Study group. Intensive treatment with methotrexate in early rheumatoid arthritis: aiming for remission. Computer Assisted Management in Early Rheumatoid Arthritis (CAMERA, an open-label strategy trial). Ann Rheum Dis. 2007;66:1443-9.
14. Sanders M. A review of controlled clinical trials examining the effects of antimalarial compounds and gold compounds on radiographic progression in rheumatoid arthritis. J Rheumatol. 2000;27:523-9.

15. Ten Wolde S, Breedveld FC, Hermans J, Vandenbroucke JP, Van de Laar MA, Markusse HM, et al. Randomised placebo-controlled study of stopping second-line drugs in rheumatoid arthritis. Lancet. 1996;347:347-52.
16. Klinkhoff A. Biological agents for rheumatoid arthritis: targeting both physical function and structural damage. Drugs. 2004;64:1267-83.
17. Furst DE, Keystone EC, Fleischmann R, Mease P, Breedveld FC, Smolen JS, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2009. Ann Rheum Dis. 2010;69(Suppl.I):i2-29.
18. Ledingham J, Deighton C, on behalf of the British Society for Rheumatology Standards, Guidelines and Audit Working Group (SGAWG). Update on the British Society for Rheumatology guidelines for prescribing TNFα blockers in adults with rheumatoid arthritis (update of previous guidelines of April 2001). Rheumatology (Oxford). 2005;44:157-63.
19. Lee SJ, Chang H, Yazici Y, Greenberg JD, Kremer JM, Kavanaugh A. Utilization trends of tumor necrosis factor inhibitors among patients with rheumatoid arthritis in a United States observational cohort study. J Rheumatol. 2009;36:1611-7.
20. Van der Heijde DM, Van't Hof M, Van Riel PL, Van der Puttle LB. Development of a disease activity score based on judgement in clinical practice by rheumatologists. J Rheumatol. 1993;20:579-81.
21. Scott DL, Kingsley GH. Tumor necrosis factor inhibitors for rheumatoid arthritis. N Engl J Med. 2006;355:704-12.
22. Ikeda K, Cox S, Emery P. Biological therapy in early arthritis – overtreatment or the way to go?. Arthritis Res Ther. 2007;9:211-7.
23. Emery P, Breedveld FC, Hall S, Durez P, Chang DJ, Robertson D, et al. Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, double-blind, parallel treatment trial. Lancet. 2008;372:375-82.
24. Emery P, Breedveld F, Van der Heijde D, Ferraccioli G, Dougados M, Robertson D, et al. Clinical remission and inhibition of radiographic progression with combination etanercept-methotrexate therapy versus monotherapy in active, early rheumatoid arthritis: 2-year results from the COMET trial. Ann Rheum Dis. 2009;68(Suppl 3):119.
25. Allaart CF, Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Breedveld FC, Dijkmans BA, FARR study group. Aiming at low disease activity in rheumatoid arthritis with initial combination therapy or initial monotherapy strategies: the BeSt study. Clin Exp Rheumatol. 2006;24(Suppl 43):S77-82.
26. Grigor C, Capell H, Stirling A, McMahon AD, Lock P, Vallance R, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. Lancet. 2004;364:263-9.
27. Bakker MF, Jacobs JW, Verstappen SM, Bijlsma JW. Tight control in the treatment of rheumatoid arthritis: efficacy and feasibility. Ann Rheum Dis. 2007;66(Suppl 3):56-60.
28. Ward MM. Interpreting measurements of physical function in clinical trials. Ann Rheum Dis. 2007;66(Suppl 3):32-4.
29. Prevoo ML, Van't Hof MA, Kuper HH, Van Leeuwen MA, Van de Putte LB, Van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. **Arthritis Rheum.** 1995;38:44-8.