Reumatol Clin. 2016;12(3):146–150

Reumatología Clínica

www.reumatologiaclinica.org

Brief Report

Diagnostic and Therapeutic Delay of Rheumatoid Arthritis and its Relationship With Health Care Devices in Catalonia. The AUDIT Study☆

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ARTICLE INFO

Article history:
Received 19 March 2015
Accepted 5 August 2015
Available online 4 April 2016

Keywords:
Early onset rheumatoid arthritis
Health care devices
AUDIT study

ABSTRACT

Objective: Diagnosis and therapy of patients with early onset rheumatoid arthritis (RA) is influenced by accessibility to specialized care devices. We attempted to analyze the impact of their availability.
Methods: We analyzed time related to diagnosis delay measuring: (1) Time from first clinical symptoms to the first visit with the rheumatologist; (2) Time from referral to the first visit of rheumatology; (3) Time between first symptom until final diagnosis; (4) Time between first symptom until the initiation of the first disease-modifying antirheumatic drug (DMARD). The presence of these 6 rheumatology devices was defined: (1) Early arthritis monographic clinics, (2) RA monographic clinics, (3) mechanisms for fast programming, (4) algorithms for referral from primary care (PC), (5) rheumatology consultation services in PC and (6) consulting services in PC.
Results: The mean time from onset of symptoms to diagnosis or the establishment of a DMARD in RA patients in Catalonia is very long (11 months). Patients seen in rheumatology devices such as RA monographic clinics, rheumatology consultation in PC and specially in early arthritis clinics are treated early with DMARDs.
Conclusion: The existence of monographic clinics or consulting in primary care centers is essential to improve early care of RA patients.

☆ Please cite this article as: Corominas H, Narváez J, Díaz-Torné C, Salvador G, Gomez-Caballero ME, de la Fuente D, et al. Retraso diagnóstico y terapéutico de la artritis reumatoide y su relación con dispositivos asistenciales en Catalunya. Estudio AUDIT. Reumatol Clin. 2016;12:146–150.

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Retraso diagnóstico y terapéutico de la artritis reumatoide y su relación con dispositivos asistenciales en Catalunya. Estudio AUDIT

Palabras clave:
Artritis reumatoide de inicio reciente
Dispositivos de asistenciales especializados
Estudio AUDIT

RESUMEN

Objetivo: Analizar el retraso diagnóstico y terapéutico en pacientes con AR de reciente comienzo en 19 centros de Catalunya.
Métodos: Encuesta epidemiológica en 183 pacientes en que se cuantificaron los tiempos en relación con el retraso diagnostico midiendo: *1)* aparición del primer síntoma hasta la primera visita a Reumatología; *2)* desde la derivación hasta la primera visita de Reumatología; *3)* entre aparición del primer síntoma hasta el diagnóstico, y *4)* entre aparición del primer síntoma hasta el inicio del primer FAME. Se definió la existencia de 6 dispositivos asistenciales diferenciados.
Resultados: El tiempo medio desde el inicio de los síntomas hasta la instauración de un FAME en pacientes con AR en Catalunya es muy largo (11 meses). Pacientes atendidos en dispositivos como consultas de AR, consultas especializadas en atención primaria y sobre todo en consultas de artritis de inicio son tratados de manera más temprana con FAME.
Conclusión: La existencia de determinados dispositivos asistenciales es fundamental para mejorar la atención precoz en la AR.

Introduction

In recent decades, the approach to the management of rheumatoid arthritis (RA) has changed the prognosis of this disease. A large body of evidence shows that early treatment (within the first 3 months) is more effective and is associated with higher remission rates, absence of radiological progression and less severe disability.[1–5]

The diagnosis and therapy vary widely in RA for a number of reasons, including patient delay in presenting to the primary care (PC) physician, delayed referral from PC to a specialist, and delay in being seen by a rheumatologist once the referral has been produced.[6] According to the Spanish emAR study (*Estudio sobre el manejo de la arteritis reumatoide* [Study of the management of rheumatoid arthritis]) published in 2007, the lag time between symptom onset and the initiation of effective treatment on the part of a rheumatologist has gradually been reduced over the past few decades, but it is still far from ideal.[7,8]

In the context of the presentation of the master plan for musculoskeletal diseases by the health department of the autonomous government of Catalonia, in northeastern Spain, (2011–2015), a working group was created to develop improvements in the early diagnosis of RA in that region. An epidemiological survey was proposed to a number of rheumatology departments (the AUDIT study) to determine: (a) the diagnostic delay ("time to diagnosis") and treatment delay ("time to treatment") of RA patients to analyze the lag times observed from symptom onset to the first treatment with disease-modifying antirheumatic drugs (DMARDs); and (b) whether the application of certain health care mechanisms in these rheumatology departments had an impact on the possibilities of early diagnosis and treatment of the disease.

Materials and Methods

We conducted a cross-sectional study during 2011 and 2012, based on an epidemiological survey administered to 10 consecutive patients from 19 centers in Catalonia who had been diagnosed with RA in 2009 or 2010. Epidemiological data of the patients (age, sex, race, city or town of residence) were recorded, as were the number and types of DMARDs received by each. We analyzed the prevalence of rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (anti-CCP), and the presence of erosions at the time of diagnosis and the time of this writing. In addition, the time variables were analyzed in relation to the delay in patient care: (1) from the onset of the first symptom to the first visit to a rheumatologist; (2) from referral to the first visit to a rheumatologist; (3) from the onset of the first symptom to the definitive diagnosis; and (4) from the onset of the first symptom to the administration of the first DMARD. For each center, we indicated whether or not it offered any of 6 rheumatology care mechanisms or features: (1) dedicated early arthritis (EA) clinic; (2) dedicated RA clinic; (3) mechanisms for early appointment scheduling; (4) algorithms for referral from PC; (5) rheumatology unit in the PC center; and (6) counseling service in PC.

Statistical methods: Student's *t* test was used for the comparison of means. The chi-squared test and Spearman correlation were utilized to analyze the correlation between the different rheumatology care features. The relationship between lag time from symptom onset to initiation of the first DMARD and the different rheumatology care features was analyzed by linear regression. The probability of a lag time of less than 6 or 12 months was analyzed using multivariate logistic regression. Those features that were marginally significant in univariate analyses ($P<.1$) were included as explanatory variables in the regression models. As these variables were correlated, they were grouped as a single variable that indicated the number of rheumatology care features that had been used by the patients (0–3). Statistical significance was established at $P<.05$. The analyses were performed with the SPSS software package (version 18).

Results

A total of 183 patients were included (132 women) with a mean age of 57.2 ± 14 years (range: 22–87), with a disease history of 27.3 ± 20 months. The disease began as palindromic rheumatism in 15.8%. Positivity for RF was detected in 73.2% and for anti-CCP in 68.6%. Only 6% (11 patients) had rheumatoid nodules; 32 patients (17.5%) had erosions on radiography at the time of diagnosis and 47 (25.7%) at the time of this writing. The DMARD most frequently administered was methotrexate, in 122 patients (73.5%), followed by leflunomide in 13%; 34 patients (18.7%) were being treated with biologic agents. In all, 71% (130 patients) had been referred from PC, 8.7% from the emergency department and the remaining 20%, from other medical services and the orthopedic department.

The time elapsed from the onset of the first symptom to the first visit to a rheumatologist was 10.2 ± 12.7 months, to the time of diagnosis of RA, 11.3 ± 13.2 months, and to the first DMARD, 11.1 ± 12.8 months. The time from referral to the first visit to a

Table 1
Disease Course According to the Available Rheumatology Care Features: Dedicated Early Arthritis Clinic.

Time elapsed (months) from. . .	Dedicated early arthritis clinic		
	Yes	No	*P*
. . .**onset to the first visit to a rheumatologist** (time from onset of 1st symptom to 1st visit to a rheumatologist)	7.5 ± 10 (0.3–66)	11.6 ± 13.7 (1–60)	.016*
. . .**patient referral to visit to a rheumatologist** (time from referral to 1st visit to a rheumatologist)	2.6 ± 2.8 (0–12)	4.2 ± 6.9 (0–59)	.213 NS
. . .**onset of symptoms to diagnosis of RA** (time from 1st symptom to diagnosis)	8.8 ± 11.4 (0.4–72)	12.6 ± 14 (1–75)	.046*
. . .**onset of 1st symptom to 1st treatment with a DMARD**	8.4 ± 10.5 (0.4–72)	12.6 ± 13.7 (0–75)	.015*

DMARD, disease-modifying antirheumatic drug; RA, rheumatoid arthritis.
* Statistically significant (*P*<.05).

Table 2
Disease Course According to the Available Rheumatology Care Features: Rheumatology Unit in Primary Care and Counseling Services.

Time elapsed (months) from. . .	Rheumatology unit in primary care (PC) and counseling services (C)		
	Yes	No	*P*
. . .**onset to the first visit to a rheumatologist**	(PC) 8.3 ± 11.9 (0.3–6)	11 ± 13.7 (1–60)	.003*
(time from onset of 1st symptom to 1st visit to a rheumatologist)	(C) 9.8 ± 13.4 (0.3–66)	10.8 ± 11.4 (1–60)	.016*
. . .**patient referral to visit to a rheumatologist**	(PC) 2.2 ± 3 (0–16)	4.2 ± 6.6 (0–59)	.001*
(time from referral to 1st visit to a rheumatologist)	(C) 3 ± 3.8 (0–22)	4.6 ± 8.2 (0–59)	.077 NS
. . .**onset of symptoms to diagnosis of RA**	(PC) 8.1 ± 9.5 (0.4–44)	12.8 ± 14.4 (1–75)	.004*
(time from 1st symptom to diagnosis)	(C) 10.3 ± 13.1 (0.4–75)	12.9 ± 13.4 (1–60)	.017*
. . .**onset of 1st symptom to 1st treatment with a DMARD**	(PC) 9.1 ± 10.3 (0.0–53)	12.1 ± 13.7 (1–75)	.056*
	(C) 10.5 ± 12.8 (0–75)	(12.2–12.9) (1–60)	.189 NS

DMARD, disease-modifying antirheumatic drug; NS, not significant; RA, rheumatoid arthritis.
* Statistically significant (*P*<.05).

rheumatologist was 3.6 ± 5.8 months. In all, 34.4% of the patients had access to a dedicated EA clinic and 37.2% to a dedicated RA clinic; early appointment scheduling was applied in 66.1% and referral algorithms in 31.1%; 31.7% were seen in a PC rheumatology department and 61.7% in a counseling or consultation service.

The existence of the above features was associated with a shorter lag time between onset of symptoms and initiation of the first DMARD, although only access to an EA clinic was significant. This clinic was also associated with a shorter lag time from symptom onset to the first visit to a rheumatologist (7.5 ± 10 months vs 11.6 ± 13.7 months; *P*=.016) and to the diagnosis of RA (8.8 ± 11.4 months vs 12.6 ± 13.7 months; *P*=.046) (Table 1). The existence of dedicated RA clinics was associated with a shorter time from onset of the first symptom to the confirmation of the diagnosis of RA (*P*=.040). The availability of counseling in the PC center was significantly associated with a shorter delay from the onset of symptoms to the first visit to a rheumatologist and to diagnosis, but not to the first DMARD. The same was observed in PC centers that had a rheumatology department although, in this case, the association with a shorter lag time following referral was very significant (Table 2). The evaluation of the 6 possible rheumatology care features showed that only the existence of dedicated EA clinics was associated with a closer proximity to treatment of RA, with a shorter time from onset of the first symptom (months) to the initiation of the first DMARD (Table 3).

For multiple regression analysis, we excluded the features that had no statistically significant relationship to the lag time from symptom onset and the initiation of the first DMARD, and included the 3 that did. As these features were correlated, they were grouped in terms of the number of patients who had had access to 1, 2 or 3 of these features. The results, shown in Table 4, indicate that the patients with access to only 1 feature had the same lag time as the patients who had not had access to any of them. However, when the patients had had access to 2 or 3 of these features, the lag time was significantly shorter (*P*=.016) or showed a trend toward significance (*P*=.107), with reductions of between 6 and 5 months. Logistic regression analysis showed that the patients with access to 2 or 3 of these features had a 2.6 (95% confidence interval [CI], 1.3–5.6) times greater probability of having a lag time of less than 12 months (*P*=.01) and a 1.8 (95% CI, 1–3.4) times greater probability of having a lag time of less than 6 months (*P*=.07).

Discussion

Successful early control of RA depends, first, on the patients, who must realize that they have the disease, assimilate the signs

Table 3
Relationship Between Time of Symptom Onset to Initiation of First Disease-modifying Antirheumatic Drug and the Rheumatology Care Features.

Rheumatology care features	Time from onset of 1st symptom (months) to initiation of 1st DMARD		
	Yes	No	*P*
Dedicated EA clinic	8.4 ± 10.5	12.6 ± 13.7	.015*
Dedicated RA clinic	9.0 ± 10.0	12.4 ± 14.1	.09 NS
Mechanism for scheduling early appointments	10.6 ± 12.1	12.3 ± 14.1	.717 NS
Counseling services in PC centers	10.5 ± 12.8	12.2 ± 12.9	.189 NS
Rheumatology unit in PC centers	9.1 ± 10.3	12.1 ± 13.7	.056
Referral algorithms	12.4 ± 15.4	10.6 ± 11.4	.84 NS

DMARD, disease-modifying antirheumatic drug; EA, early arthritis; NS, not significant; PC, primary care; RA, rheumatoid arthritis.
* Statistically significant (*P*<.05).

Table 4
Relationship Between Dedicated Early Arthritis and Rheumatoid Arthritis Clinics, Rheumatology Units in Primary Care and Time From Onset of First Symptom to First Treatment With DMARDs: Multiple Regression Analysis.

Parameters	*B* (95% CI)	*P* value
Constant	13 (10.1 to 15.9)	.000
EA or RA or PC (only 1 of the 3) vs none of the 3[a]	0.2 (−4.4 to 4.8)	.934
EA or RA or PC (2 of the 3) vs none of the 3[b]	−6 (−10.9 to −1.1)	.016
EA or RA or PC (all 3) vs none of the 3[c]	−5.3 (−11.7 to 1.2)	.107

CI, confidence interval; DMARDs, disease-modifying antirheumatic drugs; EA, early arthritis; PC, primary care; RA, rheumatoid arthritis.

[a] Patients who made use of only 1 of these rheumatology care mechanisms – dedicated EA clinic, dedicated RA clinic or rheumatology unit in PC – versus patients who did not make use of any of the 3.

[b] Patients who made use of 2 of the above rheumatology care mechanisms versus patients who did not make use of any of the 3.

[c] Patients who made use of all 3 of the above rheumatology care mechanisms versus patients who did not make use of any of the 3.

and symptoms and visit their family physicians. A second limitation corresponds to the delay in referral from their PC physicians to rheumatology specialists. It is in this second barrier that the delay produced can be excessive. There may be a variety of reasons, but the existence of mechanisms for urgent care and well-defined referral criteria are directly associated with more adequate care.[9]

In 2007, Clemente et al. analyzed the emAR Spanish cohort by reviewing the medical records of 865 patients, showing that the median time from the onset of symptoms to the first DMARD treatment was 14 months. However, they observed a reduction in the time to first DMARD over the past 2 decades (median 8 months in 1995–1999, the last period evaluated), due mostly to a reduction of the time to a visit to a specialist. Their findings contrast with those of our AUDIT study, in which we have reduced the time from referral to the visit to a rheumatologist, shortening the time to the initiation of the first DMARD to less than 1 month.[7] Despite these favorable data, the lag time between the onset of the first symptom to the visit to a rheumatologist continues to be very long, slightly greater than that reported by other authors.[9–15]

There have been attempts to identify other explanations for differences in patient management, beyond the existing mechanisms. Kumar et al. observed that the delay in delivery of care to their cohort of 169 patients was mostly due to factors depending on the perception of the disease itself.[10] Later, in 2012, an observational study in 10 representative centers in 8 European countries concluded that the delay in delivery of care to RA patients in Europe was multifactorial and unacceptably long.[11] In 2002, Palm and Purinszky attempted to show sex-related differences to explain why the 59 women with EA were referred later, on average, than men, but found no objective data.[12]

In 2010, Van der Linden et al. evaluated the cause of delay in a cohort from Leiden, classifying the causes into 2 subgroups: those due to the patients themselves and those related to PC physicians. The factors that determined the delay in being assessed were mostly clinical, such as the insidious onset of the disease, normal acute-phase reactant levels, symmetry and small joint involvement.[13] In our case, we demonstrated that closer proximity to PC physicians through counseling services favors direct interchange and referral; in contrast, the latter is delayed in centers that do not have mechanisms of urgent care.

The study of the French ESPOIR cohort, reported in 2010, evaluated the time to access to a rheumatologist in 814 patients with EA, comparing it with the European League Against Rheumatism (EULAR) recommendations, which indicate that it should be less than 6 weeks. The authors confirmed the difficulty in complying with the recommendations, and only 46.2% visited a rheumatologist within that period. As in our study and in another cohort from a metropolitan area in Canada, the differences observed were due to the barrier constituted by PC but, in contrast to the French cohort, the majority of our centers do not have features like arthritis units, a circumstance that adds to the lag time.[14,15]

The literature on inflammatory arthritis has placed little emphasis on factors that are less specific, but are of great importance in the overall management of arthritis, such as the time lost due to the patients' failure to perceive the disease, the time it takes to be seen by a specialist and the lack of specific mechanisms of urgent or preferential care, like EA clinics. This situation was referred to in 2011 by the SERAP working group; however, our report demonstrates that 2 years later, the development of these clinics in Spain was still inadequate, at least in our geographic region.[16]

The AUDIT study is the first to analyze the importance of the existence of dedicated EA and RA clinics, and evaluates these features. Quality care in RA should be based on closer proximity to PC and on the creation of dedicated clinics, taking into account that, even in those centers in which they are already established, the lag time is still too long.

Nevertheless, our study has certain limitations. Firstly, although the sample is substantial, it is not a large cohort. Secondly, the sample was not randomized, the participating centers vary widely and the study did not evaluate sociodemographic or cultural factors. Thirdly, the great majority of the centers involved do not have EA clinics, a circumstance that results in a loss of homogeneity. However, we should point out that one of the strengths of the AUDIT study is that it represents diverse care models from different geographic regions, while it also provides a survey of real-world cases that are found in clinical practice. Finally, the close correlation observed between the presence of different rheumatology care features makes an exact interpretation of the multivariate analysis difficult, although the presence of EA clinics is identified as the most relevant factor in reducing the lag time from symptom onset to the first DMARD.

The AUDIT study confirms the suspicion that the rates of earlier diagnosis and treatment are higher in centers that have dedicated EA clinics or, in their absence, dedicated RA clinics. The times to care delivery and first DMARD treatment are shorter in those centers and result in better management of these inflammatory diseases. We consider that, in Spain, the implementation of improved referral criteria, the design of better defined algorithms and, above all, the creation of dedicated EA and RA clinics would result in earlier and more effective diagnosis and treatment of RA.

Ethical Disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Funding

Project financed by Merck Sharp & Dohme de España.

Authorship

All the authors have contributed to the same extent to the project, which was promoted and sponsored by the Societat Catalana de Reumatologia (SCR).

Conflicts of Interest

The authors declare they have no conflicts of interest.

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