Orthopedic Surgery in Rheumatoid Arthritis in the Era of Biologic Therapy

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ABSTRACT. ***Objective.*** To analyze sociodemographic and clinic-related factors associated with the use of orthopedic surgical procedures in rheumatoid arthritis (RA), focusing on the potential role of new biologic therapies.

Methods. A retrospective medical record review was performed in a probability sample of 1272 patients with RA from 47 units distributed in 19 Spanish regions. Sociodemographic and clinical features, use of drugs, and arthritis-related joint surgeries were recorded following a standardized protocol.

Results. A total of 94 patients (7.4%) underwent any orthopedic surgery during their disease course, with a total of 114 surgeries; 47 (41.2%) of these surgeries were total joint replacement (TJR). The median time to first orthopedic procedure was 7.9 years from the onset of RA symptoms, and the rate of orthopedic surgery (excluding TJR) was 4.5 procedures per 100 person-years from the beginning of RA, while the rate of TJR was 2.25 interventions per 100 person-years. A higher risk of undergoing an orthopedic surgical procedure was associated with taking nonsteroidal antiinflammatory drugs (NSAID) in the previous 2 years, female sex, longterm disease, and the presence of extraarticular complications. The risk factors for undergoing a TJR were being old, having a longterm disease, and taking biologic therapies.

Conclusion. In the era of biologics, our national audit found a low percentage of patients who underwent orthopedic surgery, probably reflecting a thorough management of the RA. Sociodemographic factors, longterm RA, extraarticular complications, and NSAID were associated with orthopedic surgery. (J Rheumatol First Release Sept 15 2013; doi:10.3899/jrheum.130118)

Key Indexing Terms:
ORTHOPEDICS RHEUMATOID ARTHRITIS BIOLOGIC THERAPY

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology and autoimmune nature, with a moderately high prevalence[1] and great disease burden on patients in terms of pain, disability, and life expectancy[2,3]. RA is characterized by chronic inflammation and polyarticular destruction[4,5]. Usually damage is progressive and irreversible, and causes deterioration in physical function that is only partially recoverable with joint replacement.

Early diagnosis and aggressive treatment improve RA outcomes such as inflammation and disability[6]. However, progressive joint destruction continues in some patients, who will require orthopedic surgery during their disease course[7]. The percentage of patients with RA who undergo orthopedic surgery is quite high, representing more than half[8]. Patients undergoing an orthopedic surgery procedure have a worse prognosis in terms of disability and quality of life; in addition, they use more healthcare resources and social services, with great socioeconomic consequences[9,10,11].

The use of orthopedic interventions in RA, particularly large joint replacement, is considered a marker of disease severity and an indicator of medical management failure[6]. Several studies suggest that since 1985 there has been a decrease in the need for orthopedic surgery, likely as a result of advances in the management of RA[12,13,14,15,16,17,18]. In 2000 the emAR study (*Estudio de la variabilidad en el manejo de la artritis reumatoide en España* — Study of the variability in the management of rheumatoid arthritis in Spain) found that up to 26% of patients with RA had undergone any orthopedic procedure during their disease course. The emAR also showed that clinical variables, such as disease activity and severity, as well as geographic and socioeconomic variables, were associated with orthopedic

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surgery[19]. During the 10 years after the emAR study ended, care for patients with RA underwent a revolution, with earlier and more aggressive approaches as well as new biologic treatments. Treat-to-target strategies that focus on frequent monitoring and treatment adjustments to achieve states of low disease activity or clinical remission may have also contributed to superior longterm results[20]. This tight disease control theory has been linked to a better understanding of the processes and development of rheumatology care in our health system.

Our hypothesis was that 10 years after the emAR was conducted, a second variability study, the emAR II, should reflect changes in the management and outcome measures of RA, including orthopedic surgery rates. RA variability studies are important to understand the use of different health resources and diagnostic and therapeutic procedures, including such associated disease consequences as orthopedic surgery, to improve the management and outcomes of these patients.

The objectives of our study were (1) to describe the rates of orthopedic surgical procedures in patients with RA in Spain in recent years, and (2) to examine sociodemographic and clinic-related factors associated with the use of orthopedic procedures in this population, with attention to the potential role of new biologic therapies.

MATERIALS AND METHODS

Study design, patient sample, and data collection. The emAR II, conducted in 2010, is an audit study of the variability in the management of RA, with the same design as the previous emAR study[21]: a cross-sectional national study with retrospective review of the first year of disease plus the last 2 years of followup in rheumatology clinics throughout Spain. To have belonged to the previous cohort was not an exclusion criterion.

The study retrospectively reviewed the medical records of individuals aged ≥ 16 years and diagnosed with RA by the 1987 American College of Rheumatology (ACR) criteria[22]. They were followed at rheumatology departments of Spanish hospitals and had at least 1 visit in the previous 2 years.

The emAR II used a stratified random sampling: first by autonomous communities (regions into which Spain is administratively divided) and then by hospital (first-stage units) and patient (second-stage units). To avoid the lack of representativeness associated with the homogeneity of hospitals of very different sizes, sampling with probability proportional to size was conducted in the first stage, and equiprobable random selection of patients in each center, in the second stage.

Sample size was calculated assuming that the proportion of patients requiring orthopedic surgery may have decreased from 26% to 18% between the emAR studies, and that the change should be detected. Based on this hypothesis, we obtained a minimum sample requirement of 1410 medical records, assuming an α error of 5%, a power of 80%, a percentage of unreachable or incomplete medical records of 15%, and a design effect of 2.5.

Variables. Two primary outcomes were established for this analysis: (1) any orthopedic surgery, defined as the report in the medical record of at least 1 RA-related orthopedic surgery including primary and secondary total joint replacement (TJR) at any location, reconstructive joint surgery, resections, joint fusions, and synovectomy. Fractures or infection-related surgeries were excluded; and (2) TJR, defined as total replacement of a joint at any location from the beginning of the RA. Revision surgery was considered as a new RA-related surgery if first replacement was considered RA-related (i.e., it was not a consequence of fracture or any other condition). TJR as a consequence of fractures were not included.

To assess variability in the primary outcomes, the following predictive and confounding factors were considered: (1) sociodemographic variables including sex, age, marital status (married vs not married), educational level (any study degree vs no studies), social status (lower, middle, or upper depending on the patient's occupation according to the protocol of the Spanish Society of Epidemiology)[23]; (2) disease-related variables, including the date of RA onset and diagnosis, disease duration (short-term RA as < 10 yrs of RA duration vs longterm RA as ≥ 10 yrs disease duration), ACR functional class or grade, range of values for erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) throughout the study period, maximum and minimum number of tender and swollen joints during the study period, rheumatoid factor (RF), extraarticular complications, and comorbid medical conditions; and (3) pharmacological variables such as drugs prescribed in the last 2 years including maximum and minimum doses of disease-modifying antirheumatic drugs (DMARD), biologic agents, nonselective nonsteroidal antiinflammatory drugs (NSAID), corticosteroids, analgesics, gastric protection, and drugs for treatment or prophylaxis of osteoporosis.

To identify patients with more active disease, we constructed the variable "Activity" defined as active_ESR (ESR > 50 mm/h on 2 visits during the study period) and/or active_DAS [a minimum of 3.2 in DAS28 (28-joint Disease Activity Score) on 2 visits] and/or active_Physician (moderate or severe activity according to the rheumatologist on 2 determinations).

In addition, we used the common descriptive variables for patients with RA collected from the same source. All patient data were extracted from medical records by researchers trained in standardized data collection.

Data analysis. Patients were described using summary statistics. We estimated the rate of any orthopedic surgery and of TJR with 95% CI. Orthopedic surgery and TJR incidence rates were estimated by dividing the number of new surgeries occurring during followup by the number of person-years of exposure. Both rates are given per 100 person-years. We compared with previous cohort emAR I with a chi-squared test. Bivariate logistic regression analyses were performed to measure the association between any orthopedic surgery or TJR and secondary variables. Then 2 multivariate logistic regression models were run to identify independent predictive factors associated with orthopedic surgery or TJR. The results of the logistic regression analyses were expressed as OR. The criterion to include a variable in the multivariate models was reaching a $p < 0.10$ in the bivariate analysis. All regression models were additionally adjusted for age, sex, clinical variables, and disability.

All analyses were performed using Stata 13.0 statistical software (Stata Corp.).

RESULTS

Study population. A total of 47 patients agreed to participate in the study; 138 records were not located or were incomplete for the purposes of the study. Thus, the final sample comprised 1272 records from patients with RA, distributed in 19 Spanish regions. Missing and incomplete records were equally distributed among the regions.

Sociodemographic and clinical features of patients are shown in Table 1. A majority (73%) were women, with a median age of 63.3 years and median disease duration of almost 8 years. ESR median values ranged between 11 and 33 mm/h. Some type of comorbidity was registered in 49.4% of patients. The most common comorbidities found were hypertension (28.2%) and diabetes mellitus (10.2%). In relation to disability (ACR functional class), more than

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Table 1. Sociodemographic and clinical baseline features of the study population. Results are expressed in absolute numbers of patients and percentages except where indicated.

Age, yrs*, n = 1269	63.3 (51.6–73.3)
Age at disease onset, yrs*, n = 1019	49.8 (23.2–39.8)
Disease duration, yrs, n = 1140	4.15 (3.85–13.99)
No. women, n = 1267	928 (73.2)
RF-positive, n = 1262	944 (74.8)
CRP antibody, n = 745	511 (69.6)
Functional class (ACR) III–IV, n = 87	228 (25.7)
Erosive disease, n = 1190	738 (62)
Other clinical features, n = 1292	
Serositis	20 (1.6)
Interstitial lung disease	30 (2.3)
Rheumatoid vasculitis	12 (0.9)
Raynaud	33 (2.6)
C1-C2 subluxation	33 (2.6)
Rheumatoid nodules	152 (11.9)
Carpal tunnel syndrome	83 (6.5)
Sjögren syndrome	131 (10.3)
Scleritis	11 (0.9)
Felty syndrome	5 (0.4)
Amyloidosis	2 (0.1)

* Median (25/75 percentiles). RF: rheumatoid factor; CRP: C-reactive protein; ACR: American College of Rheumatology.

half the patients were able to perform all activities of daily living (51%), 23% had slight disability (grade II), and 25.7% had ACR functional grade III/IV. Regarding factors of poor prognosis, the proportion of patients who were RF-positive was quite high, and over half had an erosive disease. Anticyclic citrullinated peptide antibody was positive in 69.6% of patients. A total of 31.5% of patients had some extraarticular complication, the most frequent being rheumatoid nodules.

Treatments. RA treatments were recorded at every visit and are shown in Table 2. Corticosteroids were taken by 67.6% of the patients, and 67.3% took NSAID at some point during the previous 2 years. Most of the patients had been treated with DMARD, and 20.7% had taken 2 or more DMARD. A total of 36.9% of patients were prescribed any biologic treatment. The most frequent biologic treatment was etanercept, followed by adalimumab and infliximab. The median time from diagnosis to the start of biologic treatment was 59.8 months, with 25th and 75th percentiles of 23.9 and 125.7 months. The median duration of the biologic treatment was 10.3 months ($P_{25\text{-}75}$ 3.5 to 26.1).

Type and rate of orthopedic surgery. A total of 94 patients (7.4%) underwent any orthopedic surgery during their disease course, with a total of 114 first surgeries; 47 (41.2%) of these surgeries were TJR. Bilateral procedures were included and considered as separate cases. There were also 38 revision surgeries (13 of these were TJR). These were not included in subsequent analyses.

In the previous similar cohort of emAR I, a significantly higher percentage (25.9%) of the patients had any orthopedic procedure ($p < 0.0001$).

Table 2. Rheumatoid arthritis (RA) treatments of the study subjects.

Treatment	N (%)
DMARD in the last 2 yrs	
Azathioprine	7 (0.5)
Cyclosporine	7 (0.5)
Chlorambucil	1 (0.1)
Chloroquine/HCQ	190 (12.2)
D-penicillamine	—
Leflunomide	345 (22.1)
Methotrexate	930 (59.6)
Gold salts	26 (1.7)
Sulfasalazine	48 (3.1)
Administration of 2 or more DMARD	264 (20.7)
Biologic drugs during disease evolution	469 (36.9)
Abatacept, 10 mg/kg	16 (2.1)
Abatacept, other doses	7 (0.9)
Adalimumab, 40 mg	204 (27.3)
Adalimumab, other doses	6 (0.8)
Anakinra, 100 mg	5 (0.7)
Anakinra, other doses	—
Etanercept, 25 mg	91 (12.2)
Etanercept, 50 mg	149 (19.9)
Etanercept, other doses	3 (0.4)
Infliximab, 3 mg/kg	153 (20.5)
Infliximab, 5 mg/kg	14 (1.9)
Infliximab, other doses	8 (1.1)
Rituximab, 500 mg; 2 infusions	8 (1.1)
Rituximab, 1000 mg; 2 infusions	57 (7.6)
Rituximab, other doses	3 (0.4)
Tocilizumab, 4 mg	3 (0.4)
Tocilizumab, 8 mg	12 (1.6)
Tocilizumab, other doses	2 (0.3)
Corticosteroids in the last 2 yrs	860 (67.6)
NSAID in the last 2 yrs	856 (67.3)

DMARD: disease-modifying antirheumatic drugs; HCQ: hydroxychloroquine; NSAID: nonsteroidal antiinflammatory drugs.

The median time to first orthopedic procedure was 7.9 years from the onset of RA symptoms, and the rate of any orthopedic surgery (except TJR) was 4.5 procedures per 100 person-years from the beginning of RA, while the rate of TJR was 2.25 interventions per 100 person-years.

We performed a new separate analysis comparing patients who received biologic therapy with those who did not. For patients who had biologic therapy, the rate of any orthopedic surgery (except TJR) was 4.67 procedures per 100 person-years from the beginning of RA, while the rate of TJR was 3.1 interventions per 100 person-years. For patients without biologic therapy, the rate of any orthopedic surgery (except TJR) was 4.23 procedures per 100 person-years from the beginning of RA, while the rate of TJR was 2.35 interventions per 100 person-years.

Table 3 describes the location and the number of orthopedic surgeries performed. The most common types of surgery in patients with RA were TJR (41.2%), surgeries

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Table 3. Types of orthopedic procedures. Results are expressed in absolute numbers of patients and percentages.

Procedure Type	N = 1271
Patients with any orthopedic surgery	94 (7.4)
Total surgical procedures	114
Unknown procedure	2 (1.7)
Arthroscopy	4 (3.5)
Total joint replacement	47 (41.2)
Surgery without replacement	38 (33.3)
Soft tissue surgery	15 (13.2)
Spinal surgery	8 (7.0)

without replacement (33.3%), and soft tissue interventions (13.2%). Only 8 spinal surgeries (including cervical and lumbar; 7%) and 4 arthroscopies (3.5%) were performed. The most common surgical complication was infection (9.6%), but most surgeries (66.7%) were free of any complication. There were no deaths as a result of surgery.

Variables associated with undergoing any orthopedic surgery and specifically TJR. In the bivariate analysis to assess the risk of undergoing any orthopedic surgery, the variables that reached statistical significance were taking NSAID in the previous 2 years (OR 1.69, 95% CI 1.07–2.66), female sex (OR 1.86, 95% CI 1.12–3.11), longterm disease (OR 2.17, 95% CI 1.43–3.30), and the presence of extraarticular complications (OR 1.59, 95% CI 1.26–2.00). When these variables were entered into a multivariate regression model (Table 4), all remained associated with a higher risk of undergoing an orthopedic surgical procedure. The multivariate model included age, clinical disease activity, CRP, and RF for adjustment.

The same strategy of analysis was followed using as the dependent variable having had any TJR during the development of RA. First, in bivariate analyses, the variables that achieved statistical significance were age, with increased risk to older patients (OR 1.68, 95% CI 0.85–3.33), and longterm disease (over 10 yrs; OR 3.32, 95% CI 1.69–3.50). The multivariate model included sex, age, CRP, and RF for adjustment, plus others that showed some trend in the bivariate analysis, such as steroids (OR 1.68, 95% CI 0.85–3.33), biologic therapy (OR 1.66, 95% CI 0.94–2.95), and extraarticular RA (OR 1.08, 95% CI 0.55–2.10). After adjustment, being older, having a longterm disease, and having been prescribed biologic therapies fit in the final model (Table 5).

Table 4. Multivariate analysis related to any first orthopedic surgery. Only variables with $p < 0.05$ in the multivariate analysis are shown.

Variable	OR	95% CI	p
NSAID in last 2 yrs	1.78	1.07–2.97	0.02
Female	1.83	1.05–3.19	0.03
Longterm RA (≥ 10 yrs)	1.88	1.21–2.93	0.005
Extraarticular complications	1.56	1.20–2.02	0.001

NSAID: nonsteroidal antiinflammatory drugs; RA: rheumatoid arthritis.

DISCUSSION

The need for orthopedic interventions in RA, particularly replacement of large joints, is considered a marker of disease severity and an indicator of medical management failure. In our study we described the trend for orthopedic surgical procedures in patients with RA in Spain. There was a marked decrease in the percentage of patients who underwent any orthopedic surgery in the biologic era, and if we compared our results with a similar previous cohort[19], rates declined from 25.9% to 7.4%, with an OR 0.79 and a decrease of 20% in the rate ratio.

The study was done in a very representative sample of patients with RA. There were not only Spanish patients with RA, but also other European patients with RA, because sociodemographic and clinical characteristics are quite similar[24].

From the middle of the 1990s through 2010, RA management underwent several changes, the first of which was the window of opportunity concept and then the tight-control theory[13,25]. The use of methotrexate has consistently increased, and it is now established as the leading DMARD[26,27]. Moreover, early, aggressive, combined therapy, optimization doses of DMARD, and the use of biologics have become popular in Western countries, representing new, radical approaches in RA treatment[27,28,29]. These changes enable a tighter control of disease activity, and as a result, the clinical outcomes of patients with RA have been consistently improving. We demonstrated that surgery is being performed earlier after the onset of symptoms (4 yrs earlier compared with emARI)[9]. There was a marked decrease in the percentage of patients who underwent orthopedic surgery, going from 25.9% to 7.4% compared to studies conducted several years ago, probably reflecting a thorough management of the disease[9,14,15,16,17,18,19,20]. This improved management seems to be reflected also in functional status, measured with ACR class or grade, with a lower percentage of patients having ACR functional grade III/IV (25.7 vs 33.1%) as compared to previous studies[19].

Biologic therapies appeared at first as an option for patients with more severe diseases and DMARD failure and

Table 5. Multivariate analysis related to total joint replacement. Only variables with $p < 0.05$ in the multivariate analysis are shown.

Variable	OR	95% CI	p
Age, per yr	1.03	1.006–1.06	0.01
Longterm RA (≥ 10 yrs)	2.90	1.44–5.84	0.003
Biologic therapy	1.95	1.01–3.86	0.04

RA: rheumatoid arthritis.

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especially with established joint damage, which may explain the increase of risk of TJR in patients taking biologic therapy. However, this trend has changed, and biologic therapies are replacing other therapeutic options such as switching or adding classical DMARD to achieve remission in recently diagnosed patients. This shift to biologic therapies may explain the decrease in the overall rate of orthopedic surgeries compared with our previous data. In our cohort, patients with the greatest structural damage were treated with biologic therapy but that did not reverse the damage, and ultimately they needed TJR.

Thus in recent decades, the disease has a better prognosis. This improvement may reflect early diagnosis and adequate treatment rather than a change in characteristics of the disease process[30]. In fact, a few variables, as well as some sociodemographic nonmodifiable factors independently associated with orthopedic surgery, remain similar to those previously found. As has been reported, women with RA are more likely to undergo orthopedic surgery than men[2,3,9,31,32,33], reflecting a greater extent of the disease among women and perhaps a higher social burden, different patterns of pain perception, or cosmetic concerns.

Age was also related to greater probability of TJR. The aging of the total population, as a result of advances in medical treatment, among other causes, means that there is a growing number of older patients with RA who have major damage due to joint degeneration. These patients undergo an increased number of surgical operations related to aging, to preserve their function and quality of life. Longterm RA and extraarticular complications remain as risk factors for orthopedic surgery in emAR II.

The use of NSAID also emerged as a risk factor for orthopedic surgery in our study. The patient may experience improvement in pain and joint function with NSAID, but erosion is not prevented, thus leading to the orthopedic surgery.

Biologic therapies have arisen as an option for patients with more severe disease and DMARD failure. Most of them have established joint damage, which may explain the increase in risk of TJR in patients taking biologic therapy. This is probably a result of the change in treatment trends, which has considered the biologic/DMARD combined as a second or third choice for poorly controlled patients[34,35,36], replacing other therapeutic options such as switching or adding classical DMARD. However, because the greatest structural damage occurs within the first 2 years from the onset of symptoms[37], biologic therapies slow down the disease but do not reverse the damage.

The recent rapid advances in drug therapy have had significant consequences, as this study shows; the number of surgeries has drastically declined compared with emAR I[9]. In the near future, this trend may continue. Further advances in drug therapy and management could reduce the severity of bone-joint destruction related to RA. This may contribute to a decrease in the amount of RA-related joint surgery, especially joint replacements. However, the general population, and therefore patients with RA, will be getting older in the coming years, and the number of elderly patients needing orthopedic surgery related to aging will increase.

The main limitation of our study is that it was a retrospective cross-sectional method based on medical record review and not designed so much to identify predictive factors for surgery as to determine actual trends in orthopedic surgery. However, the results of this study can be extrapolated to the whole population of Spain.

Despite the decrease of orthopedic surgeries through modifiable factors, patients undergoing an orthopedic surgery have a worse prognosis related to disability and quality of life. Thus, further advances are needed in earlier diagnosis and therapeutic intervention, as well as tight control, to avoid progressive joint destruction. Moreover, orthopedic surgery in patients with RA represents a significant part of the cost of the disease[10], and it is still necessary to work to reduce the number of orthopedic surgeries in patients with RA.

APPENDIX

List of members of the emAR Study Group: Alegre J, Alonso JL, Alvarez M, Alvárez B, Aragón A, Arasa FX, Arias MJ, Beltrán J, Babío J, Bohorquez C, Boquet D, Bustabad S, Casado A, Calvet J, Castro S, Colazo MR, Collantes E, Cuende E, Chozas N, Delgado E, de la Fuente D, de Juanes A, del Rincón E, Enríquez E, Escudero C, Espadaler L, Espino P, Fernández A, Fernández J, Fernández L, Fiter J, Font P, Galvez J, Gallego A, García J, García J, García ME, Gamero F, Giménez E, Gómez S, González Álvarez B, González S, Granados M, Iglesias G, Irigoyen V, Jimenez F, Júdez E, López C, López M, López R, López-Longo FJ, Maese J, Manero-Ruiz FJ, Manrique S, Maries I, Martínez C, Martínez-Cristóbal A, Mateo I, Marzo J, Medina F, Medina J, Medrano M, Mesa P, Miguélez R, Monteagudo I, Montilla C, Moreno I, Muñoz ML, Naranjo A, Negueroles R, Nolla M, Ojeda S, Ordás C, Ordóñez S, Ortíz AM, Pagán E, Pecondón A, Esteban S, Pérez-Pampín E, Pina JM, Piqueras JA, Pozuelo MJ, Rios V, Rivera N, Rodríguez C, Rodríguez JM, Roselló R, Rubira MJ, Ruiz D, Saiz E, Sánchez M, Tinturé T, Tornero C, Tornero J, Úcar E, Ureña I, Vázquez C, Veroz R, Vicente E, and Zubieta J.

REFERENCES

1. Carmona L, Villaverde V, Hernandez-Garcia C, Ballina J, Gabriela R, Laffon A. The prevalence of rheumatoid arthritis in the general population of Spain. Rheumatology 2002;41:88-95.
2. Wolfe F, Hawley DJ. The longterm outcomes of rheumatoid arthritis: Work disability: a prospective 18 year study of 823 patients. J Rheumatol 1998;25:2108-17.
3. Escalante A, del Rincon I. How much disability in rheumatoid arthritis is explained by rheumatoid arthritis? Arthritis Rheum 1999;42:1712-21.
4. Harris ED. Rheumatoid arthritis. Pathophysiology and implications for therapy. N Engl J Med 1990;322:1277-89.
5. Machold KP, Stamm TA, Nell VP, Pflugbeil S, Aletaha D, Steiner G, et al. Very recent onset rheumatoid arthritis: clinical and serological patients characteristics associated with radiographic progression over the first years of disease. Rheumatology 2007;46:342-9.
6. Breedveld FC, Kalden JR. Appropriate and effective management

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of rheumatoid arthritis. Ann Rheum Dis 2004;63:627-33.
7. James D, Young A, Kulinskaya E, Knight E, Thompson W, Ollier W, et al. Orthopedic intervention in early rheumatoid arthritis. Occurrence and predictive factors in an inception cohort of 1064 patients followed for 5 years. Rheumatology 2004;43:369-76.
8. Kapetanovic MC, Lindqvist E, Saxne T, Eberhardt K. Orthopedic surgery in patients with rheumatoid arthritis over 20 years: prevalence and predictive factors of large joint replacement. Ann Rheum Dis 2008;67:1412-6.
9. Lajas C, Abasolo 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.
10. Newhall-Perry K, Law NJ, Ramos B, Sterz M, Wong WK, Bulpitt KJ, et al. Direct and indirect costs associated with the onset of seropositive rheumatoid arthritis. Western Consortium of Practicing Rheumatologists. J Rheumatol 2000;27:1156-63.
11. Stone CE. The lifetime economic costs of rheumatoid arthritis. J Rheumatol 1984;11:819-27.
12. Da Silva E, Duran FM, Crowson CS, O'Fallen WM, Matteson EL. Declining use of orthopedic surgery in patients with rheumatoid arthritis? Results of a long-term, population-based assessment. Arthritis Rheum 2003;49:216-20.
13. Weiss RJ, Stark A, Wick MC, Ehlin A, Palmblad K, Wretenberg P. Orthopaedic surgery of the lower limbs in 49,802 rheumatoid arthritis patients: results from the Swedish National Inpatient Registry during 1987 to 2001. Ann Rheum Dis 2006;65:335-41.
14. Weiss RJ, Ehlin A, Montgomery SM, Wick MC, Stark A, Wretenberg P. Decrease of RA-related orthopaedic surgery of the upper limbs between 1998 and 2004: data from 54,579 Swedish RA inpatients. Rheumatology 2008;47:491-4.
15. Verstappen SM, Hoes JN, Ter Borg EJ, Bijlsma JW, Blaauw AA, Albada-Kuipers GA, et al. Joint surgery in the Utrecht Rheumatoid Arthritis Cohort: the effect of treatment strategy. Ann Rheum Dis 2006;65:1506-11.
16. Pedersen A, Johnsen S, Overgaard S, Søballe K, Sørensen HT, Lucht U. Total hip arthroplasty in Denmark: incidence of primary operations and revisions during 1996-2002 and estimated future demands. Acta Orthop 2005;76:182-9.
17. Fevang B, Lie S, Havelin L, Engesaeter LB, Furnes O. Reduction in orthopedic surgery among patients with chronic inflammatory joint disease in Norway, 1994–2004. Arthritis Rheum 2007; 57:529-32.
18. Momohara S, Ikari K, Mochizuki T, Kawamura K, Tsukahara S, Toki H, et al. Declining use of synovectomy surgery for rheumatoid arthritis patients in Japan. Ann Rheum Dis 2009;68:291-2.
19. Loza E, Abásolo L, Clemente D, López-González R, Rodríguez L, Vadillo C, et al. Variability in the use of orthopedic surgery in patients with rheumatoid arthritis in Spain. J Rheumatol 2007;34:1485-90.
20. Sen D, Brasington R. Tight disease control in early RA. Rheum Dis Clin North Am 2012;38:327-43.
21. Lopez-Gonzalez R, Hernandez-Garcia C, Abasolo L, Morado I, Lajas C, Vadillo C, et al. emAR Study Group. Differences between rheumatology attending physicians and training residents in the management of rheumatoid arthritis in Spain. Scand J Rheumatol 2008;37:419-26.
22. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.
23. Alonso J, Perez P, Saez M, Murillo C. [Validity of the occupation as an indicator of social class, according to the British Registrar General classification][Spanish]. Gac Sanit 1997;11:205-13.
24. Sokka T, Kautiainen H, Toloza S, Makinen H, Verstappen SM, Lund Hetland M, et al. QUEST-RA: quantitative clinical assessment of patients with rheumatoid arthritis seen in standard rheumatology care in 15 countries. Ann Rheum Dis 2007;66:1491-6.
25. Raza K, Saber TP, Kvien TK, Tak PP, Gerlag DM. Timing the therapeutic window of opportunity in early rheumatoid arthritis: proposal for definitions of disease duration in clinical trials. Ann Rheum Dis 2012;71:1921-3.
26. Yazici Y. Long-term safety of methotrexate in the treatment of rheumatoid arthritis. Clin Exp Rheumatol 2010;5 Suppl 61;S65-7.
27. Saeki Y, Matsui T, Saisho K, Tohma S. Current treatments of rheumatoid arthritis: from the 'NinJa' registry. Expert Rev Clin Immunol 2012;8:455-65.
28. Scott DL. Biologics-based therapy for the treatment of rheumatoid arthritis. Clin Pharmacol Ther 2012;91:30-43.
29. Jain A, Stein BE, Skolasky RL, Jones LC, Hungerford MW. Total joint arthroplasty in patients with rheumatoid arthritis: a United States experience from 1992 through 2005. J Arthroplasty 2012;27:881-8.
30. Welsing PM, Fransen J, van Riel PL. Is the disease course of rheumatoid arthritis becoming milder? Time trends since 1985 in an inception cohort of early rheumatoid arthritis. Arthritis Rheum 2005;52:2616-24.
31. Anderson RJ. The orthopedic management of rheumatoid arthritis. Arthritis Care Res 1996;9:223-8.
32. Massardo L, Gabriel SE, Crowson CS, O'Fallon WM, Matteson EL. A population based assessment of the use of orthopedic surgery in patients with rheumatoid arthritis. J Rheumatol 2002;29:52-6.
33. Reilly PA, Cosh JA, Maddison PJ, Rasker JJ, Silman AJ. Mortality and survival in rheumatoid arthritis: a 25 year prospective study of 100 patients. Ann Rheum Dis 1990;49:363-9.
34. Castañeda S, Navarro F, Fernández-Carballido C, Tornero C, Marced E, Corteguera M. [Differences in the management of early and established rheumatoid arthritis] [Spanish]. Reumatol Clin 2011;7:172-8.
35. Bykerk VP, Akhavan P, Hazlewood GS, Schieir O, Dooley A, Haraoui B, et al. Canadian Rheumatology Association recommendations for pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs. J Rheumatol 2012;39:1559-82.
36. Bombardier C, Hazlewood GS, Akhavan P, Schieir O, Dooley A, Haraoui B, et al. Canadian Rheumatology Association recommendations for the pharmacological management of rheumatoid arthritis with traditional and biologic disease-modifying antirheumatic drugs: part II safety. J Rheumatol 2012;39:1583-602.
37. van der Heijde DM, van 't Hof M, van Riel PL, van de Putte LB. Development of a disease activity score based on judgment in clinical practice by rheumatologists. J Rheumatol 1993;20:579-81.

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