Orthopedic Surgery in Rheumatoid Arthritis: Results from the Spanish National Registry of Hospitalized Patients over 17 Years

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ABSTRACT. ***Objective.*** To analyze the trend of orthopedic surgery (OS) rates on patients with rheumatoid arthritis (RA).

Methods. Retrospective observational study based on information provided by the Spanish National System of Hospital Data Surveillance. All hospitalizations of patients with RA for orthopedic surgery [total hip arthroplasty (THA), total knee arthroplasty (TKA), arthrodesis, and upper limb arthroplasty (ULA)] during 1999–2015 were analyzed. The age-adjusted rate was calculated. Generalized linear models were used for trend analysis.

Results. There were 21,088 OS in patients over 20 years of age (77.9% women). OS rate adjusted by age was 754.63/100,000 RA patients/year (women 707.4, men 861.1). Neither an increasing nor a decreasing trend was noted for the total OS. However, trend and age interacted, so in the age ranges 20–40 years and 40–60 years, an annual reduction of 2.69% and 2.97%, respectively, was noted. In the age ranges over 80 years and 60–80 years, we noted an annual increase of 5.40% and 1.09%, respectively. The average age at time of OS increased 5.5 years during the period analyzed. For specific surgeries, a global annual reduction was noted in rates for arthrodesis. In THA, there was an annual reduction in patients under 80 years. In TKA and ULA, there was an annual reduction in patients under 60 years.

Conclusion. Although the overall OS rate has not changed, there is a decrease in the rate of arthrodesis at all ages, THA in patients under 80 years of age, as well as TKA and ULA in patients under 60 years of age. (First Release November 15 2019; J Rheumatol 2020;47:341–8; doi:10.3899/jrheum.190182)

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Rheumatoid arthritis (RA), a systemic autoimmune disease mainly affecting diarthrodial joints, is one of the most debilitating forms of arthritis and affects about 0.5–2% of the world's population[1]. RA is characterized by functional incapacity, joint damage, reduced quality of life, and early death. RA is 2–4× more common in women than men[2]. In serious or uncontrolled RA, inflammation may lead to irreparable joint damage[1,3,4]. In terminal stages, the only treatment available for joint damage is surgical replacement of the damaged joint or arthrodesis[5]. A UK study showed that the accumulated disease burden, based on DAS28 scoring, during the first 5 years post-RA diagnosis predicted the need for major joint surgery[3]. Moreover, the highest surgery incident rates were observed among patients with moderate and high disease activity[3]. These findings support the importance of aggressive early treatment emphasized in current RA treatment guidelines. In older RA patient cohorts, over 50% of patients were found to require joint surgery during the course of their disease[6,7].

RA treatment has progressed significantly in the last 20 years because of early application and a strategy aimed at achieving disease remission. Advances in the understanding of RA pathogenesis have evolved significantly during this period and have led to the introduction of biological therapies and new strategies in RA management such as treat to target (T2T)[8], although it is not clear whether this has translated into lower rates of orthopedic surgery (OS). The majority of studies suggest a reduction in OS incidence post-introduction of biological therapies[5,9,10,11,12,13]. However, studies have also been published showing no changes or even an increase in the number of OS[5,12,14,15].

Using data from the national registry of hospitalizations in Spain (CMBD), our aim was to research the likely effect of this new RA treatment paradigm on the incidence rate and trend of certain OS, such as total hip arthroplasty (THA), total knee arthroplasty (TKA), arthrodesis, and upper limb arthroplasty (ULA) in patients with RA.

MATERIALS AND METHODS

This was a retrospective population study based on analyzing the administrative data collected in a basic minimum set of data from all hospitals in Spain, provided by the Ministry for Health. This database encompasses administrative data (date of admission, hospital, financing system, place of residence, and others), demographic data (sex, age, town, region, death while hospitalized), clinical data (personal history and diagnosis on discharge), and procedures (e.g., tests or interventions performed during hospitalization) of all hospitalizations in Spain. This database uses a uniform code for all hospital discharge reports and its completion is compulsory for all hospitals, both private and public.

The CMBD uses the clinical codes of the Spanish version of the International Classification of Diseases, 9th ed (ICD-9), includes admission to any national hospital (public or private), and is estimated to cover 99.5% of the Spanish population[16]. We have assumed that the remaining population and hospitalization information not included in the study follow the same epidemiological characteristics.

We requested from the Ministry for Health (ICD-9: 714.0- 714.9) data on all hospitalizations in which the primary or secondary diagnosis was RA during the period January 1, 1999, to December 31, 2015. The different OS were identified by their respective codes (ICD-9) involving any procedure position: THA 81.50-81.53, TKA 81.54-81.55, arthrodesis of upper or lower limb joints 81.20-81.29, and ULA: elbow and shoulder 81.80-81.88 and hands 81.70-81.79. Available administrative, demographic, and clinical data were included for each registry. The Charlson Comorbidity Index was obtained through the ICD-9 codes, following the methodology recommended by Deyo, *et al*[17]. The formula used by this methodology is the original[18]. In general, the absence of comorbidity corresponds to 0 or 1 point, low comorbidity 2 points, and high comorbidity more than 3 points. Age groups were established as follows: 20–39 years, 40–59 years, 60–79 years, and over 80 years.

Statistical methods. For the total OS and for each of those included (THA, TKA, ULA, and arthrodesis), crude yearly rates were calculated (/100,000 RA-patients/year) by sex and age group. The numerator of this rate is the number of cases registered at the CMBD and the risk population denominator. The risk population was estimated based on the national census provided by the National Statistics Institute (INE — Spanish acronym) and assumed an RA prevalence of 0.5% (both sexes): 0.8% in women and 0.2% in men. This RA prevalence is the same as that estimated in the EPISER study[19].

Adjusted rates using the direct method were also calculated according to age, estimated with a 95% CI using 2015 as the reference population.

The change in annual rates (linear trend) was analyzed by generalized linear models with a Poisson distribution or negative binomial distribution in cases of overdispersion. To assess trends according to age groups, the models include a first-tier level of interaction effect. Estimated rates are presented for models with their corresponding 95% confidence level. Analyses were performed for all samples and strata according to sex.

Quantitative data are described with average and SD. Categorical data are expressed with absolute and relative frequencies. In the univariant analysis, the chi-square test was performed for qualitative variables, and the Student t test or the Mann-Whitney U test, according to data distribution, in the case of quantitative variables. All tests were considered bilateral, with a significance level of $p < 0.05$.

Statistical analysis was performed using IBM SPSS 24.0, Epidat 4.2, and Stata 14 packages.

This study was approved by the Hospital U. Fundación Alcorcón Ethics Research Committee (reference number 17/48).

RESULTS

There was a total of 338,343 hospitalizations of patients with RA throughout the 17-year study period corresponding to a total of 176,097 patients (117,985 women and 58,112 men). Of the patients, 21,088 (6.2%) involved hospitalizations for OS, 8709 (2.6%) THA, 9006 (2.7%) TKA, 1372 (0.4%) arthrodesis, and 2230 (0.7%) ULA. By sex, 16,432 (77.92%) were women and 4656 (22.07%) were men. The average age was 65.02 (SD 13.26) years. The average stay was 10.97 (SD 12.55) days. The Charlson Index average was 1.26 (SD 0.71); 1.34 (SD 0.84) for men and 1.23 (SD 0.66) for women ($p < 0.001$). A total of 125 (0.6%) patients died during hospitalization; 38 (0.81%) of whom were men and 87 women (0.52%, $p = 0.079$). Table 1 shows the main characteristics according to OS type.

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Table 1. Description of the patients with RA who underwent an orthopedic surgery, between 1999 and 2015.

Characteristics	All OS	THA	TKA	AA	ULA
n (% of all hospitalizations)	21,088 (6.2)	8709 (2.6)	9006 (2.7)	1372 (0.4)	2230 (0.7)
Women, n (%)	16,432 (100)	6545 (39.83)	7117 (43.31)	1118 (6.8)	1846 (11.23)
Men, n (%)	4656 (100)	2164 (46.80)	1889 (40.57)	254 (5.46)	384 (8.25)
Age, yrs, mean (SD)	65.02 (13.26)	66.57 (14.78)	65.97 (10.90)	55.90 (13.12)	59.93 (12.50)
ALHS, mean (SD)	10.97 (12.55)	13.48 (13.50)	10.73 (11.20)	6.69 (18.60)	4.54 (4.69)
Charlson Comorbidity Index, mean (SD)	1.26 (0.71)	1.33 (0.80)	1.25 (0.60)	1.08 (0.50)	1.13 (0.70)
In-hospital death, n (%)	125 (0.60)	104 (1.20)	20 (0.20)	1 (0)	1 (0)

RA: rheumatoid arthritis; OS: orthopedic surgery; THA: total hip arthroplasty; TKA: total knee arthroplasty; AA: arthrodesis; ULA: upper limb arthroplasty; ALHS: average length of hospital stay.

The average age (of all OS) increased by 5.5 years during this 17-year study period, from 61.8 years (SD 13.8) in 1999 to 67.3 years (SD 12.8) in 2015 ($p < 0.05$). Figure 1 shows the evolution of average age for the different surgeries.

The age-adjusted rate of OS total was 754.63/100,000 RA-patients/year (95% CI 713.15–798.04) during the study period, being greater in men (861.18, 95% CI 761.85–970.97) than in women (707.49, 95% CI 663.57–753.72). The crude and adjusted rates per year are shown in Table 2.

Neither an increasing nor decreasing trend in the global rate of OS was observed during the study period (Figure 2). However, we did find a statistically significant correlation with age. Thus, by age strata, the results were as follows: in the over 80 years and 60–80 years groups, an annual increase of 5.40% (IRR 1.054, 95% CI 1.040–1.068) in the former and 1.1% (IRR 1.011, 95% CI 1.003–1.019) in the latter were recorded. In the age strata 20–40 years and 40–60 years, an annual decrease was observed of 2.69% (IRR 0.973, 95% CI 0.959–0.987) and 2.97% (IRR 0.970, 95% CI 0.962–0.979), respectively (Table 3 and Figure 2).

THA. Regarding hip arthroplasty in women, there was a nonsignificant annual age-adjusted rate reduction of 0.69% (IRR 0.993, 95% CI 0.980–1.006), whereas in men there was a nonsignificant annual increase of 0.42% (IRR 1.004, 95% CI 0.994–1.014). By age strata, we observed an annual reduction of 2.05% in the 20–40 year range (IRR 0.979, 95% CI 0.962–0.997), an annual reduction of 3.55% (IRR 0.964, 95% CI 0.955–0.974) in the 40–60 year range, and an annual reduction of 0.99% (IRR 0.99, 95% CI 0.981–0.999) in the 60-80 year range. Last, in patients over 80, there was an annual increase of 4.64% (IRR 1.046, 95% CI 1.031–1.062; Table 3 and Figure 3).

Knee arthroplasty. Annual age-adjusted rates by age for knee prostheses in men increased 1.51% (IRR 1.015, 95% CI 1.004–1.027) while in women there was a nonsignificant increase of 0.65% (IRR 1.006, 95% CI 0.993–1.020). By age range, it was noted that in the 20–40 year range, there was an annual reduction of 3.79% (IRR 0.962, 95% CI 0.946–0.979), in the 40–60 year range the annual reduction was 2.86% (IRR 0.971, 95% CI 0.961–0.982), in the 60–80

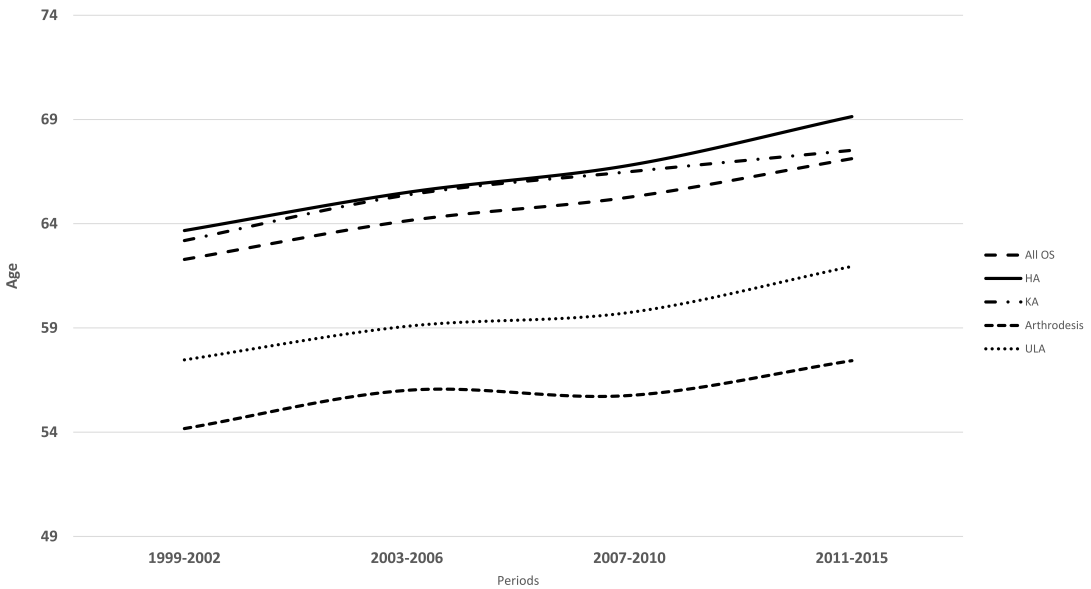

Figure 1. Evolution of average age between 1999 and 2015, globally and per surgery type. OS: orthopedic surgery; HA: hip arthroplasty; KA: knee arthroplasty; ULA: upper limb arthroplasty.

Table 2. Crude and adjusted incidence per OS type in both sexes.

Yr	RA	No. OS				Crude IR/100,000 RA–Patients/Yr				Age-adjusted IR/100,000 RA–Patients/Yr			
	Population, n	THA	TKA	AA	ULA	THA	TKA	AA	ULA	THA	TKA	AA	ULA
1999	154,688	382	372	75	76	246.95	240.48	48.48	49.13	263.33	251.60	50.28	51.30
2000	156,458	507	395	81	85	324.05	252.46	51.77	54.33	347.22	262.29	54.99	56.96
2001	158,163	469	443	87	98	296.53	280.09	55.01	61.96	312.09	294.14	56.91	64.66
2002	164,981	539	497	84	128	326.70	301.25	50.92	77.58	359.93	323.87	54.92	83.67
2003	168,509	480	437	125	129	284.85	259.33	74.18	76.55	316.23	279.72	81.36	83.23
2004	171,559	465	493	90	132	271.04	287.36	52.46	76.94	301.18	309.22	57.13	84.16
2005	175,149	541	537	73	127	308.88	306.60	41.68	72.51	341.34	333.80	45.46	78.94
2006	178,059	543	576	79	159	304.96	323.49	44.37	89.30	339.29	347.07	48.32	96.81
2007	181,634	546	551	86	123	300.60	303.36	47.35	67.72	332.72	329.42	50.29	73.27
2008	184,555	500	559	86	128	270.92	302.89	46.60	69.36	297.44	328.53	49.97	74.76
2009	185,995	493	539	76	156	265.06	289.79	40.86	83.87	288.31	311.85	42.91	90.01
2010	186,762	516	527	86	155	276.29	282.18	46.05	82.99	298.56	300.76	48.75	87.88
2011	187,416	510	567	60	135	272.12	302.54	32.01	72.03	289.66	319.44	33.61	75.87
2012	187,508	547	564	56	132	291.72	300.79	29.87	70.40	306.70	314.00	30.72	72.96
2013	186,853	560	597	70	141	299.70	319.50	37.46	75.46	309.67	328.44	38.34	77.60
2014	186,298	554	698	87	167	297.37	374.67	46.70	89.64	301.62	379.66	47.16	90.81
2015	186,069	559	654	71	159	300.43	351.48	38.16	85.45	300.43	351.49	38.16	85.45

OS: orthopedic surgery; RA: rheumatoid arthritis; THA: total hip arthroplasty; TKA: total knee arthroplasty; AA: arthrodesis; ULA: upper limb arthroplasty.

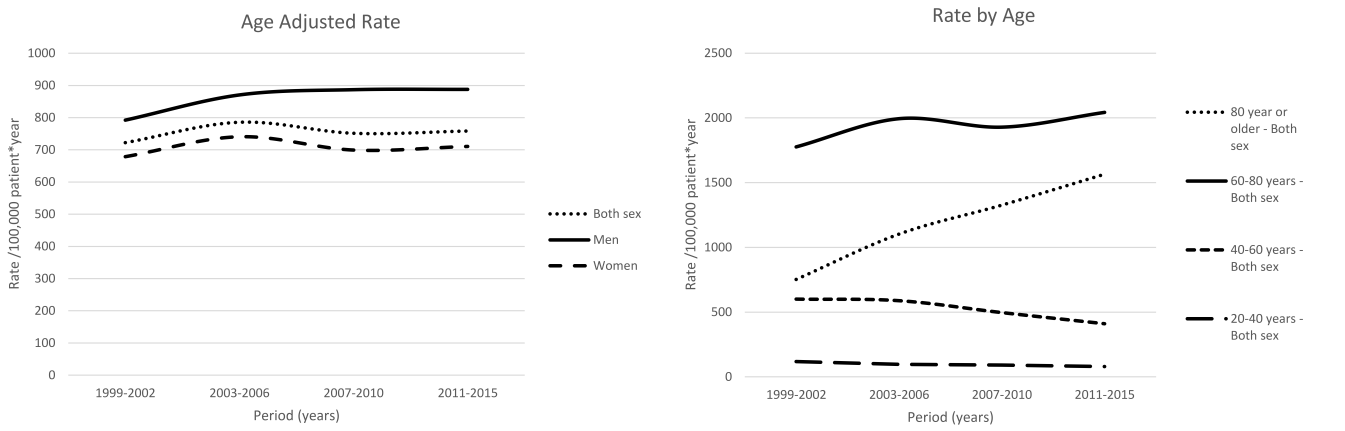

Figure 2. Trend of global orthopedic surgery and by age ranges.

year range there was an annual increase of 2.56% (IRR 1.026, 95% CI 1.018–1.034), and in the over 80 age range an annual increase of 6.75% (IRR 1.067, 95% CI 1.043–1.092; Table 3 and Figure 3).

Arthrodesis. Annual age-adjusted rates by age for arthrodesis dropped 2.89% (IRR 0.971, 95% CI 0.944–0.999) in men and 3.04% (IRR 0.97, 95% CI 0.957–0.983) in women (Table 3 and Figure 3).

ULA. In the annual age-adjusted rates by age for upper limb prosthesis, there was an increase of 1.58% (IRR 1.016, 95% CI 1.001–1.031) in women, while in men there was a nonsignificant increase of 1.78% (IRR 1.018, 95% CI 0.989–1.047). By age strata, we observed a nonsignificant annual reduction of 1.57% (IRR 0.984, 95% CI 0.954–1.015) in the 20–40 year range, a nonsignificant annual reduction of 1.06 (IRR 0.989; 95% CI 0.968–1.011) in the 40–60 year range, an annual increase of 3.30% (IRR 1.033, 95% CI 1.019–1.048) in the 60–80 year range, and an annual increase of 10.68% (IRR 1.107; 95% CI 1.063-1.153) in the over 80 range (Table 3 and Figure 3).

DISCUSSION

A long period was analyzed in this national-level study (1999–2015), enabling us to research trends in certain OS in patients with RA throughout Spain. The demographic characteristics (age and sex) of the sample were as expected. The initial hypothesis of our study was to assess whether the introduction of new therapeutic strategies in treating patients with RA, in tandem with strict disease controls and the use of biological therapies during the last 20 years, had had a

Table 3. Orthopedic surgery trend (THA, TKA, AA, and ULA) by sex, age ranges, and surgery type.

Variables	Annual Trend, %	IRR	95% CI	p
All OS				
Men	0.74	1.007	0.998–1.017	0.137
Women	0.17	1.002	0.990–1.014	0.781
20–40 yrs	–2.69	0.973	0.959–0.987	< 0.001
40–60 yrs	–2.97	0.970	0.962–0.979	< 0.001
60–80 yrs	1.09	1.011	1.003–1.019	0.007
> 80 yrs	5.40	1.054	1.040–1.068	< 0.001
THA				
Men	0.42	1.004	0.994–1.014	0.412
Women	–0.69	0.993	0.980–1.006	0.288
20–40 yrs	–2.05	0.979	0.962–0.997	0.024
40–60 yrs	–3.55	0.964	0.955–0.974	< 0.001
60–80 yrs	–0.99	0.990	0.981–0.999	0.028
> 80 yrs	4.64	1.046	1.031–1.062	< 0.001
TKA				
Men	1.51	1.015	1.004–1.027	0.01
Women	0.65	1.006	0.993–1.020	0.352
20–40 yrs	–3.79	0.962	0.946–0.979	< 0.001
40–60 yrs	–2.86	0.971	0.961–0.982	< 0.001
60–80 yrs	2.56	1.026	1.018–1.034	< 0.001
> 80 yrs	6.75	1.067	1.043–1.092	< 0.001
AA				
Men	–2.89	0.971	0.944–0.999	0.045
Women	–3.04	0.970	0.957–0.983	< 0.001
ULA				
Men	1.78	1.018	0.989–1.047	0.223
Women	1.58	1.016	1.001–1.031	0.034
20–40 yrs	–1.57	0.984	0.954–1.015	0.315
40–60 yrs	–1.06	0.989	0.968–1.011	0.333
60–80 yrs	3.30	1.033	1.019–1.048	< 0.001
> 80 yrs	10.68	1.107	1.063–1.153	< 0.001

IRR: incidence rate ratio; OS: orthopedic surgery; THA: total hip arthroplasty; TKA: total knee arthroplasty; AA: arthrodesis; ULA: upper limb arthroplasty.

favorable effect on OS rates. Based on our analysis, the answer is probably affirmative. Although the overall OS rate has not changed, the data supporting this conclusion are reflected in the global reduction in arthrodesis rates, measuring about 3% a year in both men and women. In addition, we found a reduction in THA in those 80 years and under, a reduction in TKA and ULA rates in the under 60s, and an average age increase of 5.5 years when OS were performed in 1999 in relation to 2015. Further, these results contrast with others from the 1980s, in which an important increase in OS was observed in the general population[20,21,22,23].

In our study, we found that in the under-60s age strata, there was a reduced trend in all OS rates (THA, TKA, arthrodesis, ULA). Moreover, this reduction in THA was also observed in the 60- to 80–year range. This trend may reflect observations by different studies on the reduction in the use of healthcare resources in patients with RA during the last 20 years. This was observed chiefly in the topic analyzed in our paper, namely OS[5,10,24,25,26,27,28] and the number of hospitalizations[29,30]. Nevertheless, the apparent association with the introduction of T2T and biological treatments is weak[31]. Although we can confirm the time association with this trend, our study design does not allow us to establish any direct link with the introduction of strategies of strict disease activity controls or the use of biological therapies, because these variables were not included in our database. In our study, however, we noticed that surgery rates for TKA and ULA in patients over 60 and for THA in those over 80 continued to rise. This probably reflects the fact that these procedures are established treatments for hip and knee arthrosis. Further, the global rates for the entire population have increased considerably since the beginning of the 1980s in many countries with aging populations[20,21,22,23]. Despite advances in medical treatment, the overall population aging, among other causes, means there is a growing number of elderly RA patients with degenerative joint damage secondary to RA. These patients typically undergo a larger number of age-related surgeries to preserve their function and quality of life[28]. Nevertheless, another analysis (unpublished) that examined 345,000 hospitalizations, as well as 18,000 patients with RA who died, determined not only the average age of hospitalized patients but also that the age of death was around 5 years greater during this same time period.

As with other studies[32], of the 4 surgeries we analyzed, only arthrodesis showed a global reduction trend in both men and women. Arthrodesis rates decreased partly because the surgical technique for joint replacement has improved substantially during the last 20 years. Currently, elbow, ankle, shoulder, and other arthroplasties are routinely performed, rather than arthrodesis of these joints.

In recent decades, patients with RA seem to have received more positive prognoses. This improvement may reflect both early diagnosis and correct treatment, as opposed to any changes in the aggressive characteristics of this disease[33]. In fact, some variables and nonmodifiable sociodemographic factors separately associated with OS remain similar to those identified previously. Unlike those reported on in other papers[6,28,33,34,35,36], the men with RA in our study had an older crude and age-adjusted rate than women. This may reflect a difference in the attention paid to male and female patients, with the former group typically demanding less. Another possible explanation is that the RA prevalence estimation of 0.2% of men in Spain[19] is too low.

OS in patients with RA can be considered a disease treatment failure marker. In prospective followup studies of patients with recent RA onset, the prevalence of OS during disease progression was 17% over a 5-year followup period[37] and 48% during a 16-year followup period[38]. These prospective studies were performed in the era prior to the availability of biological therapies. This situation has very likely undergone a considerable improvement.

Our study has both strengths and limitations, and its main

Figure 3. Trend of rates per age range and surgery type. HA: hip arthroplasty; KA: knee arthroplasty; ULA: upper limb arthroplasty.

strength lies in the large sample size over a longer period together with a standardized methodology maintained throughout the study period. The duration of the study period coupled with the exhaustive data from the CMBD provide sufficient internal validity, which in quantitative terms can be observed in the constant frequency detected each year. This is also true of its qualitative aspects and in its identification of age groups at greater risk.

Regarding limitations of our research: this was a retrospective observational study, which prevented us from establishing any causal relationships based on the results obtained. Moreover, even though the CMBD provided information on a hospital network encompassing over 99% of the Spanish population, some OS may have eluded the identification area provided by the public hospital discharge registry. In addition, there may have been some coding disparities and/or problems. There is also the possibility of OS cases in patients with RA in which RA has not correctly coded, which would result in an underestimation of our findings. Another important limitation is that the CMBD hospitalization discharge database does not include any data related to patients' exact treatment regimens.

We observed a global reduction trend for arthrodesis in THA in subjects under 80, and in TKA and ULA in subjects under 60 among patients with RA in Spain. Similarly, we noted an increase in the average age at OS of 5.5 years during the period studied.

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