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Letters to the Editor

Rate of remission among rheumatoid arthritis patients being treated by rheumatologists in routine practice

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The goal of treatment for rheumatoid arthritis (RA) is to achieve remission [1,2]. The prevalence of clinical remission can be gauged from patient registries, but they do not reflect RA in a broad sense and is available pertains to the Nordic countries [3–8]. The aim of this study is to determine the proportion of patient in remission and the treatments used in RA as managed in routine practice by rheumatologists.

This cross-sectional study was conducted between September 2016 and March 2017 in the rheumatologists of the Auvergne region in France working outside the university hospital (Study allowance IRB: CPP Sud Est 6 (2016/CE14)). Consecutive RA patients over a period of 3 months were included. The data collected included: tender joint count (TJC) and swollen joint count (SJC) out of 28 joints, joint pain on a visual analog scale (VAS, 0–10), overall disease activity according to the patient (VAS, 0–10) [9], and to the physician (VAS, 0–10), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level and the current treatment.

Overall 15/27 rheumatologists returned 455 sheets (Table 1). Almost 1/4 of the patients were on corticosteroids, 97% were being treated with a DMARD, 80% with methotrexate, and 30% with a biological therapy, with 22% receiving anti-tumor necrosis factor (anti-TNF) therapy. The proportion of patients in remission varied considerably depending on the criteria used, between 32% with the American College of Rheumatology and European League Against Rheumatism (ACR/EULAR) and 62% with DAS28-ESR (Disease Activity Score) criteria. At least 80% had low disease activity regardless of the criteria used (Table 2). Around a half of patients were in remission (VAS disease activity ≤ 1) according to the physicians or the patients. Agreement was moderate to good between the ACR/EULAR and the Simplified Disease Activity Index (SDAI) (K = 0.70) and Clinical Disease Activity Index (CDAI) criteria (K = 0.72), and weak between the ACR/EULAR and the DAS28-ESR criteria (K = 0.41). The physicians' (K = 0.48–0.68) and patients' (K = 0.46–0.69) assessments did not correlate well with the remission criteria and agreement between physicians and patients was moderate (K = 0.65). On multivariate analysis, the variables associated with remission according to the patients were the pain VAS (OR = 0.21 [0.14–0.31]) and the physician's VAS disease activity (OR = 0.41 [0.27-0.61]) but not the TJC, SJC, ESR or CRP. According

Table 1
Patient characteristics and current treatment.

Women, *n* (%)	330/447 (73.8)
Age (years) mean ± SD	64.8 ± 12.6
RA duration (years), median [IQR]	7 [4-14]
Rheumatoid factor, n (%)	337/436 (77.3)
Anti-CCP antibodies, n (%)	309/411 (75.2)
Number of painful joints (0-28, mean ± SD	1.28 ± 2.4
Number of swollen joints (0-28), mean ± SD	1.10 ± 2.0
Pain (VAS 0-10), mean ± SD	2.11 ± 2.03
Disease activity – patient (VAS 0-10), mean ± SD	2.08 ± 2.02
Disease activity – physician (VAS 0-10) mean ± SD	1.81 ± 1.86
ESR (mm 1 h), mean ± SD	14.2 ± 14.8
CRP (mg/dl), median [IQR]	1 [1;7]
Corticosteroids, *n* (%)	110/451 (24.4)
Dose (mg/d), median [IQR]	5 [4; 6]
Methotrexate, *n* (%)	364/453 (80.4)
Dose (mg/d) median [IQR]	15 [10; 15]
SC administration, *n* (%)	144/354 (40.7)
Leflunomide, *n* (%)	20/453 (4.4)
Hydroxychloroquine, *n* (%)	50/453 (11)
Sulfasalazine, *n* (%)	11/453 (2.4)
Anti-TNF[a], *n* (%)	99/453 (21.9)
Other biological therapy[b], *n* (%)	40/453 (8.9)
≥ 1 DMARD, *n* (%)	439/453 (96.9)
≥ 2 DMARDs, *n* (%)	158/453 (34.9)

SD: standard deviation; RA: rheumatoid arthritis; anti-CCP: anti-cyclic citrullinated peptide; VAS: visual analog scale; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; SC: subcutaneous; anti-TNF: anti-tumor necrosis factor; DMARD: disease-modifying antirheumatic drug.

[a] Etanercept: *n* = 65, certolizumab: *n* = 16, adalimumab: *n* = 13, infliximab: *n* = 4, golimumab *n* = 1.

[b] Tocilizumab: *n* = 16, abatacept: *n* = 12, rituximab: *n* = 12.

Table 2
Proportion of patients in remission or with low disease activity according to the different criteria.

Criteria	Remission	Low disease activity
DAS28-ESR ≤ 2.6, *n* (%)	240/390 (61.5)	309/390 (79.2)
DAS28-CRP ≤ 2.4, *n* (%)	252/422 (59.7)	
DAS28-CRP ≤ 2.1, *n* (%)	198/422 (46.9)	
SDAI ≤ 3.3, *n* (%)	169/421 (40.1)	337/421 (80.0)
CDAI ≤ 2.8, *n* (%)	160/444 (36.0)	362/444 (81.5)
ACR/EULAR, *n* (%)	144/453 (31.8)	
ACR/EULAR simplified[a], *n* (%)	176/450 (39.1)	
3v ACR/EULAR[b], *n* (%)	234/422 (55.5)	
Remission – physician (VAS ≤ 1), *n* (%)	237/449 (52.8)	
Remission – patient (VAS ≤ 1), *n* (%)	212/448 (47.3)	

DAS: disease activity score; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; SDAI: simplified disease activity index; CDAI: clinical disease activity index; ACR: American College of Rheumatology; EULAR: European league against rheumatism; VAS: visual analog scale; TJC: tender joint count; SJC: swollen joint count.

[a] The simplified ACR/EULAR criteria exclude CRP.

[b] 3v ACR/EULAR take TJC ≤ 1 and SJC ≤ 1 and CRP ≤ 1 mg/dL.

to the physicians, the variables were SJC (OR = 0.43 [0.32–0.59]), TJC (OR = 0.53 [0.37–0.75]) and the patient's VAS disease activity (OR = 0.46 [0.34–0.62]), but not the ESR, CRP or joint pain VAS. The patients in remission according to the DAS28-ESR and ACR/EULAR criteria, compared to patients not in remission, were younger, were treated less with corticosteroids and more with anti-TNF therapy but the difference was not significant regarding biologics generally.

Finally, the management of RA by rheumatologists in routine practice complied with the guidelines, since almost all of the RA patients were receiving a DMARD, some 80% had at least achieved low disease activity, and around a half (between 30 and 60%, depending on the criteria) were in remission.

Authors contribution

Drs. Dominique Meyer, Denis Verriere, Sylvie Melac Ducamp, Baptiste Glace, Florence Demarquilly, Milly Gendey, Bernard Maillet, Karim Zbadi, Christine Voquer, Jean Paul Monghal, Abdelkarim Kabchou, Julie Ledoux Eberst, Stella Cechetti, Jean Meloux, Marielle Vayssade are investigators in the study and are co-authors of this article.

Disclosure of interest

The authors declare that they have no competing interest.

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Uptrend in mortality from systemic connective tissue diseases: A joinpoint regression analysis among the general population of Brazil, 1996–2016

Previous population-based studies of mortality trends related to connective tissue diseases (CTDs) have focussed their analyses on a single systemic disorder [1–3]; hence, they failed to capture the dynamics of mortality in the general population from the large spectrum of systemic CTDs. Therefore, we performed a nationwide population-based study to primarily assess the temporal trend of mortality with CTDs overall as underlying cause in Brazil from 1996 to 2016 [the earliest and latest years to date with national-level mortality data available according to the International Classification of Diseases, 10th revision (ICD-10)] [4].

For this study, population and death counts (corresponding ICD-10 codes for systemic CTDs: M30-M36) across age groups were both obtained from the Ministry of Health at www.datasus.saude.gov.br. Annual age-standardised mortality rates (ASMRs, per 100,000 population) for all CTDs, the major disease categories, and all other ICD-10 causes (i.e., non-CTD causes) were calculated via the direct method using the 2000 US general population as standard [Appendix A, Document S1; see the supplementary material associated with this article online]. Then, a joinpoint regression analysis (program version 4.6.0.0) was conducted to examine temporal trends in ASMRs [5]. Briefly, the joinpoint model:

- identifies the time points (calendar years) at which the change in the slope of the ASMR is statistically significant, i.e., the joinpoints;
- estimates the regression function with joinpoints previously identified, i.e., determines the magnitude of the change by estimating the average annual percent change (APC) in mortality rate [6].

Over the study period, deaths related to systemic CTDs ($n = 27{,}305$; 79% women and 61% at age 20–59 years) accounted for 0.12% of fatalities ($n = 22{,}366{,}860$) in the Brazilian general population. When comparing years 1996 and 2016, significant increases were found in the proportion of deaths from systemic CTDs among men (16% [$n = 131/810$] to 22% [$n = 383/1764$]; $P = 0.001$, Chi^2) and the elderly (≥ 60 years old) (20% [$n = 164/807$] to 33% [$n = 587/1764$]; $P < 0.0001$, Chi^2). The ASMR (standard error) for all CTDs increased from 0.67 (0.03) in 1996 to 0.98 (0.02) in 2016 (46% cumulative increase). In contrast, the ASMR for non-CTD causes declined by 17% over the same time (1087.89 [1.29] to 906.43 [0.83]).

Results of the joinpoint trend analysis (Table 1 and Fig. 1) showed that although the ASMR for non-CTD causes continuously decreased from 1996 to 2016 at an APC of −1.1% (95% CI: −1.4% to −0.8%), the ASMR for all CTDs increased, on average, at an APC of 2.0% (95% CI: 0.9% to 3%) (APC, 95% CI of 4.2% [2.8% to 5.7%], 1996–2008 and −1.3% [−3.2% to 0.6%],