



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Impact of the COVID-19 pandemic on therapeutic management of rheumatoid arthritis in Brittany (France)



Early during the SARS-CoV-2 sanitary crisis, the vulnerability of patients treated with immunomodulatory agents or non-steroidal anti-inflammatory drugs (NSAIDs) with regards to the most severe forms of the disease have been suggested [1,2]. Despite rapid clarifications from health authorities and expert societies regarding the indication to continue ongoing therapy in most situations, the usual immunosuppressive treatment of several clinical conditions, including inflammatory rheumatic diseases, may have been impacted by these scientific data and their media relay [3–6]. In

the present work, our objectives were to evaluate the impact of COVID-19 pandemic on therapeutic management of rheumatoid arthritis (RA) and to identify factors associated with patient's choice to reduce or stop Disease-modifying anti-rheumatic drugs regimen (DMARD).

For this, we conducted a cross-sectional single-center study in Brittany (France) between April 23, 2020 and July 28, 2020. The study received approval from the Brest University Hospital Ethics committee (29BRC20.0110). A questionnaire was administered to patients with a diagnosis of RA satisfying ACR/EULAR criteria, receiving DMARD or having a prescription to initiate such treatment, during face-to-face or remote consultations. The

Table 1

Characteristics of overall population and results of logistic regression analyses comparing participants according to the personal decision to modify DMARD treatment in relation to the context of sanitary crisis.

| | Overall participants (n = 252) | Personal decision to reduce or stop DMARD treatment (n = 24) | No personal decision to reduce or stop DMARD treatment (n = 225) | Univariate analysis odds ratios | Multivariate analysis odds ratios |
|--|-----------------------------------|--|--|------------------------------------|--------------------------------------|
| General characteristics | | | | | |
| Age (years) | 61.3 (12.7) | 53.8 (13.3) | 62.2 (12.5) | 0.95 (0.92 to 0.98)*** | |
| Age categories | | | | | |
| 18 to 44 years | 32 (12.7%) | 6 (25.0%) | 26 (11.6%) | 1 (referent) | 1 (referent) |
| 45 to 64 years | 110 (43.9%) | 15 (62.5%) | 93 (41.5%) | 0.70 (0.25 to 1.98) | 0.77 (0.27 to 2.22) |
| 65 years and older | 109 (43.4%) | 3 (12.5%) | 105 (46.9%) | 0.12 (0.03 to 0.52)*** | 0.15 (0.03 to 0.64)** |
| Female | 191 (75.8%) | 20 (83.3%) | 169 (75.1%) | 1.66 (0.54 to 5.05) | |
| BMI (kg/m ²) | 25.3 (5.0) | 25.2 (4.8) | 25.3 (5.1) | 1.00 (0.91 to 1.10) | |
| Urban residency | 80 (32.7%) | 10 (43.5%) | 69 (31.5%) | 1.67 (0.70 to 4.00) | |
| Active smoking | 51 (20.2%) | 4 (16.7%) | 47 (20.9%) | 0.76 (0.25 to 2.32) | |
| Medical history | | | | | |
| High blood pressure | 69 (27.5%) | 3 (12.5%) | 66 (29.5%) | 0.34 (0.10 to 1.19)* | 0.44 (0.12 to 1.58) |
| Diabetes | 11 (4.4%) | 0 (0.0%) | 11 (4.9%) | Not applicable | |
| MACE | 32 (12.7%) | 2 (8.3%) | 30 (13.3%) | 0.59 (0.13 to 2.64) | |
| Chronic lung disease | 68 (28.1%) | 5 (21.7%) | 63 (29.0%) | 0.68 (0.24 to 1.91) | |
| Severe infection | 47 (18.8%) | 4 (16.7%) | 42 (18.7%) | 0.87 (0.28 to 2.67) | |
| Malignancy | 28 (11.2%) | 1 (4.2%) | 27 (12.1%) | 0.32 (0.04 to 2.44) | |
| RA characteristics | | | | | |
| Disease duration (years) | 14.9 (10.8) | 13.2 (10.8) | 15.1 (10.8) | 0.98 (0.94 to 1.02) | |
| RF positivity | 194 (79.5%) | 18 (75.0%) | 175 (80.3%) | 0.74 (0.28 to 1.97) | |
| ACPA positivity | 200 (83.0%) | 18 (75.0%) | 181 (84.2%) | 0.56 (0.21 to 1.52) | |
| Erosive disease | 162 (66.4%) | 16 (66.7%) | 145 (65.9%) | 1.38 (0.52 to 3.67) | |
| Past glucocorticoid exposure (≥ 5 mg per day for more than 3 months) | 151 (62.9%) | 14 (58.3%) | 135 (63.1%) | 0.82 (0.35 to 1.93) | |
| RA treatments | | | | | |
| Methotrexate | 164 (65.6%) | 15 (62.5%) | 149 (66.2%) | 0.85 (0.36 to 2.03) | |
| Hydroxychloroquine | 8 (3.2%) | 1 (4.2%) | 7 (3.1%) | 1.35 (0.16 to 11.4) | |
| Other synthetic DMARD | 23 (9.2%) | 3 (12.5%) | 20 (8.9%) | 1.46 (0.40 to 5.31) | |
| Biological DMARD | 140 (56.0%) | 13 (54.2%) | 126 (56.0%) | 0.93 (0.40 to 2.16) | |
| Targeted synthetic DMARD | 10 (4.0%) | 1 (4.2%) | 9 (4.0%) | 1.04 (0.03 to 8.57) | |
| Glucocorticoids | 62 (24.8%) | 8 (33.3%) | 53 (23.6%) | 1.62 (0.66 to 4.00) | |
| NSAIDs | 45 (18.1%) | 5 (20.8%) | 40 (17.9%) | 1.20 (0.42 to 3.42) | |

Reported values are mean (standard deviation) for continuous variables, numbers (percentage) for dichotomous variables. ACPA: anti-citrullinated protein antibody; BMI: body mass index; CI: confidence interval; DMARD: disease modifying anti-rheumatic drug; MACE: major adverse cardiac events; NSAID: non-steroidal anti-inflammatory drug; PGA: patient global assessment; RF: rheumatoid factor. * P-value < 0.20 (P-values < 0.20 in univariate analysis were included in the multivariate model); ** P-value < 0.05; *** P-value < 0.001.

<https://doi.org/10.1016/j.jbspin.2021.105179>

1297-319X/© 2021 Société française de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.

primary outcome was DMARD treatment modification in relation to the pandemic. Logistic regression was performed in order to identify factors associated with patient's decision to modify DMARD treatment. The explanatory variables included in the multivariate regression model were those showing P -value < 0.20 in univariate analysis. Significance was defined as $P < 0.05$ for variables in the final model. Data analyses were performed using Statistical package for the social sciences version 23.0 (IBM, Armonk, NY, USA).

Two hundred and fifty two patients participated in this survey, of which 75.8% (191/252) were women. Detailed characteristics of participants, including those related to medical background, RA characteristics and ongoing immunomodulatory therapy at last visit are provided in [Table 1](#).

Of the patients, 2.8% (7/252) reported a history of SARS-CoV-2 infection at the time of the survey. Among them, only one case was further confirmed with RT-PCR. Overall, 11.2% of patients (28/249) reported that their DMARD treatment have been transiently reduced or stopped in relation to the context of sanitary crisis. Modification of the DMARD treatment was the result of a patient's choice in 85.7% of cases (24/28). Within the same period, DMARD treatment was reduced or stopped for other reasons in 7.6% (19/249) of participants. Logistic regression analyses showed that patient's decision to modify DMARD treatment was less frequent among participants aged 65 years or over ([Table 1](#)).

This study shows that in a French area of low viral circulation, the sanitary crisis led to DMARD treatment modification in around 10% of RA patients, a result of the same order as what has been observed elsewhere in comparable contexts [7–10]. Our results describe the therapeutic modifications that can be highlighted during a classic interview with patients but do not take into account the more complex problematic of non-compliance. In most cases, treatment modification was the consequence of a patient's decision rather than a decision driven by a health-care professional. Future studies will have to determine the longitudinal impact of COVID-19 pandemic on RA optimal management.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgements

We would like to thank the clinical research department ("Direction de la recherche clinique et de l'innovation") of the Brest teaching hospital (CHU de Brest), and particularly Marie-Hélène Lallier, for their assistance in the implementation of this project. We also thank all the participants.

References

- [1] Giollo A, Adami G, Gatti D, et al. Coronavirus disease 19 (COVID-19) and non-steroidal anti-inflammatory drugs (NSAID). *Ann Rheum Dis* 2020; <http://dx.doi.org/10.1136/annrheumdis-2020-217598>.
- [2] FitzGerald GA. Misguided drug advice for COVID-19. *Science* 2020;367:1434. <http://dx.doi.org/10.1126/science.abb8034>.

- [3] Richez C, Flipo R-M, Berenbaum F, et al. Managing patients with rheumatic diseases during the COVID-19 pandemic: the French society of rheumatology answers to most frequently asked questions up to May 2020. *Joint Bone Spine* 2020;87:431–7. <http://dx.doi.org/10.1016/j.jbspin.2020.05.006>.
- [4] Francesconi P, Cantini F, Profili F, et al. COVID-19 epidemiology in rheumatic diseases in Tuscany: a case-control study. *Joint Bone Spine* 2021;88:105131. <http://dx.doi.org/10.1016/j.jbspin.2021.105131>.
- [5] Quartuccio L, Valent F, Pasut E, et al. Prevalence of COVID-19 among patients with chronic inflammatory rheumatic diseases treated with biologic agents or small molecules: a population-based study in the first two months of COVID-19 outbreak in Italy. *Joint Bone Spine* 2020;87:439–43. <http://dx.doi.org/10.1016/j.jbspin.2020.05.003>.
- [6] Richez C, Lazaro E, Lemoine M, et al. Implications of COVID-19 for the management of patients with inflammatory rheumatic diseases. *Joint Bone Spine* 2020;87:187–9. <http://dx.doi.org/10.1016/j.jbspin.2020.03.010>.
- [7] Fragoulis GE, Evangelatos G, Arida A, et al. Treatment adherence of patients with systemic rheumatic diseases in COVID-19 pandemic. *Ann Rheum Dis* 2020;80:e61. <http://dx.doi.org/10.1136/annrheumdis-2020-217935>.
- [8] Pineda-Sic RA, Galarza-Delgado DA, Serna-Peña G, et al. Treatment adherence behaviors in rheumatic diseases during COVID-19 pandemic: a Latin American experience. *Ann Rheum Dis* 2020. <http://dx.doi.org/10.1136/annrheumdis-2020-218198> [Published Online First: 23 June 2020].
- [9] Hassen LM, Almaghlouth IA, Hassen IM, et al. Impact of COVID-19 outbreak on rheumatic patients' perceptions and behaviors: a cross-sectional study. *Int J Rheum Dis* 2020;23:1541–9. <http://dx.doi.org/10.1111/1756-185X.13959>.
- [10] Khabbazi A, Kavandi H, Paribanaem R, et al. Adherence to medication in patients with rheumatic diseases during COVID-19 pandemic. *Ann Rheum Dis* 2020. <http://dx.doi.org/10.1136/annrheumdis-2020-218756> [Published Online First: 07 September 2020].

Baptiste Queré^a

Alain Sarau^b

Thierry Marhadour^a

Sandrine Jousse-Joulin^a

Divi Cornec^c

Camille Houssais^a

Guillermo Carvajal Alegria^c

Maxime Quiviger^a

Margot Le Guillou^a

Valérie Devauchelle-Pensec^c

Dewi Guellec^{d,*}

^a Rheumatology department, CHU de Brest, Brest, France

^b Rheumatology department, CHU de Brest, University of Brest, Inserm, UMR1227, Lymphocytes B et autoimmunité, University of Brest, Inserm, LabEx IGO, Brest, France

^c Rheumatology department, CHU de Brest, University of Brest, Inserm, UMR1227, Lymphocytes B et autoimmunité, Brest, France

^d Rheumatology department, CHU de Brest, Inserm, CIC 1412, Brest, France

* Corresponding author.

E-mail address: dewi.guellec@chu-brest.fr

(D. Guellec)

Accepted 12 March 2021
Available online 27 March 2021