Correspondence on 'Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 global rheumatology alliance physician-reported registry' by Gianfrancesco M *et al*. The impact of cardiovascular comorbidity on COVID-19 infection in a large cohort of rheumatoid arthritis patients

We read with interest the paper published by Gianfrancesco *et al*[1] describing the epidemiological findings associated with hospitalisation for COVID-19 in 600 patients with rheumatic diseases. Multivariate adjusted models proved a significant increased risk of hospitalisation for older age (>65 years), prednisone doses of ≥10 mg/day and presence of comorbidities, such as cardiovascular (CV) and lung diseases or diabetes. The use of biological or targeted synthetic disease-modifying antirheumatic drug (DMARD) appeared to decrease hospitalisation risk.

Underlying CV comorbidities seem to increase the susceptibility to SARS-CoV-2 infection and to contribute to myocardial injury, arrhythmia, acute coronary syndrome and venous thromboembolism also in non-rheumatic patients.[2 3] Pathophysiological mechanisms underlying cardiac injury in patients with SARS-CoV-2 infection are poorly understood. However, biological features of SARS-CoV-2 and its interaction with the immune system seem to have a pivotal role in organ damage and, in particular, in CV manifestations.[3]

Clinical and demographic characteristics of patients with rheumatic disease suffering from COVID-19 have been explored by several Italian groups, with the highest number of COVID-19 cases observed in the North, particularly in Lombardy. In this setting, Fredi *et al*, on behalf of the Brescia Rheumatology COVID-19 Study Group,[4] confirmed that patients with COVID-19 were older and more likely to have arterial hypertension and obesity, while no association with CV disease was reported by Monti *et al*[5] in 320 cases observed in Pavia.

The *Cardiovascular and Obesity and Rheumatic DISeases* (CORDIS) Study Group of the Italian Society of Rheumatology is an ongoing longitudinal observational study aiming to assess CV comorbidity and related risk factors in patients with chronic rheumatic diseases. Since January 2019, a prospective unselected cohort of patients with rheumatoid arthritis (RA) fulfilling the 2010 European League Against Rheumatism/American College of Rheumatology classification criteria, recruited in 10 University tertiary Italian Centres, has been included in the study. Demographic, clinical and serologic features, as well as ongoing treatment, were collected, and CV risk was estimated by the European cardiovascular disease risk assessment model Systematic COronary Risk Evaluation (SCORE) chart.

From 25 February to 15 July 2020, we assessed the incidence and outcomes of SARS-CoV-2 infection in our cohort, during the outpatient visit or by telemedicine visit. The prevalence of COVID-19 in general reference population was taken from the WHO website (http://www.who.int/emergencies/diseases/novel-coronavirus-2019/situaton-reports/).

We compared the study population with the general reference population by Fisher's exact test. A p value of <0.05 was considered significant. The OR was then calculated with 95% CI. As part of the GISEA Registry, the study was approved by all local ethics committees.

Overall, 1471 patients with RA (78.5% female; mean age 60±11 years; median disease duration 115 (IQR 150–186) months) were included in the analysis. The median (IQR) 10-year CV risk by SCORE algorithm was 0.8% (0.2–2.4), and 84 (6%) patients presented a high CV SCORE risk (≥5%).

We recorded six cases of SARS-CoV-2 infection confirmed by nasal pharyngeal swab (table 1); the incidence of SARS-CoV-2 infection was 4.08/1000 patients, similar to that observed in the overall Italian population. All infected patients had a disease duration >10 years and were overweight, four were affected by hypertension and/or dyslipidaemia, two by diabetes mellitus and one patient reported smoke habit. The median 10-year CV SCORE risk was 1.5 (IQR 0.5–5.75). Three patients were hospitalised for interstitial pneumonia and all completely recovered within 3 weeks.

Patients older than 65 years had a significant higher risk of SARS-CoV-2 infection (OR 10.1 (95%CI 1.4 to 119), p=0.01). Interestingly, patients with a high SCORE risk (≥5%) had an eightfold increased risk of infection (OR 8.2 (95%CI 1.5 to 35.5), p=0.04). Finally, biologic DMARD treatment did not significantly increase the risk of SARS-CoV-2 infection (OR 7 (95%CI 0.98 to 83), p=0.08).

The results of the present analysis demonstrated that the overall incidence of COVID-19 infection in a large cohort of patients with RA from different Italian regions is comparable with the general population; moreover, our data confirmed an increased risk of COVID-19 infection in patients older than 65 years, with long-standing disease and CV comorbidity, particularly in patients with a high 10-year SCORE CV risk. We also confirmed that ongoing treatment with biological therapies would not seem to affect the risk of infection in these patients, as reported in other Italian cohorts.[6]

Although the added value of the study by Gianfrancesco *et al*[1] was the identification of risk factors for hospitalisation in patients with rheumatic diseases, we believe that some points deserve further attention in these patients.[7] In particular, considering dissimilar patients' behaviours and adherence to recommendations to avoid social contacts[8] as well as the high proportion of asymptomatic subjects, large serological studies may help estimate the real spread of SARS-CoV-2 infection in patients with rheumatic diseases. Our data could also suggest further investigation on mechanisms underlying the increased risk and worst CV outcome of patients with rheumatic disorders infected by SARS-CoV-2.

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Table 1 Clinical characteristics of six patients with rheumatoid arthritis with confirmed SARS-CoV-2 infection

Patient	1	2	3	4	5	6
Age, years	65	79	62	76	70	71
Gender	Female	Male	Male	Male	Female	Female
Disease duration, years	33	11	12	26	15	11
RF/ACPA	Pos/Pos	Neg/Neg	Neg/Neg	Neg/Pos	Pos/Neg	Pos/Pos
csDMARD	MTX	MTX	LFM	–	MTX	–
bDMARD	Etanercept	–	Golimumab	Adalimumab	Adalimumab	Abatacept
cs/bDMARDs suspended	Yes	No	Yes	No	Yes	No
Prednisone, mg/day	–	7.5	5	–	5	5
BMI	30	27	25.4	25.7	26.8	27.5
Smoke	No	No	No	No	No	Yes
Comorbidity	Diabetes	Hypertension Atrial fibrillation	Dyslipidaemia	Hypertension Diabetes Dyslipidaemia	Hypertension	Hypertension
10-year CV risk SCORE (%)	8	5	0.5	1.5	0.5	1.5
Nasopharyngeal swab	Pos	Pos	Pos	Pos	Pos	Pos
IgG SARS-CoV-2	NA	Pos	Pos	Pos	Pos	NA
Infection symptoms	Fever Anosmia Arthralgia Rhinorrhea Diarrhoea	Fever Heartburn	Fever Non-productive cough Diarrhoea Headache	Asymptomatic (contact with a positive relative)	Fever Fatigue Arthralgia/Myalgia Anosmia Dyspnoea at rest	Fever Dyspnoea at rest Non-productive cough
Pneumonia at chest X-ray	No	No	Yes	No	Yes	No
Respiratory failure	No	No	No	No	No	No
Hospitalisation	No	Yes	Yes	No	Yes	No
PaO_2/FiO_2 ratio PaO_2 at BGA (mm Hg) O_2 saturation (%)	–	423 88 97	414 87 97	–	410 86 96	–
SARS-CoV-2 treatment	None	None	HCQ Azithromycin	None	HCQ Azithromycin	HCQ
Outcome	Healing	Healing	Healing	Healing	Healing	Healing
Time to discharge, days	–	16	9	–	14	–

ACPA, anti-citrullinated protein antibodies; b, biological; BGA, blood gas analysis; cs, conventional synthetic; CV, cardiovascular; DMARDs, disease modifying antirheumatic drug; HCQ, hydroxychloroquine; Neg, negative; O_2, oxygen; Pos, positive; RF, rheumatoid factor; SCORE, Systematic COronary Risk Evaluation.

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