Letter to the Editor

Chronic related group classification system as a new public health tool to predict risk and outcome of COVID-19 in patients with systemic rheumatic diseases: A population-based study of more than forty thousand patients

Since the COVID-19 outbreak, public health authorities have looked for the best evidence on infection risk and prognosis to guide their choices. The interpretation of the observational studies that variably reported increased infection rates and a poor prognosis in patients with systemic rheumatic diseases (SRD) has been limited by factors such as the selection of patients in the care of tertiary referral centres, the small available sample sizes for the less prevalent diseases, the description of SRDs as a single broad category, and the neglected influence of comorbidities [1].

The use of big healthcare data has become essential in gathering crucial information for a reliable identification of high-risk groups. The Chronic Related Group (CReG) system is an experimental approach of classification of chronic patients created to predict the medical resources needed to ensure their care. This system automatically assigns a diagnosis to a subject according to medical administrative records over a pre-set period. Specifically, CReG system relies on the registration and integration of disease-specific codes used to determine the share of healthcare costs, hospital discharge diagnoses codes and access to the prescription of drugs or therapeutic procedures uniquely associated with a specific condition [2,3].

In this analysis, we compared incidences and 30-day outcomes of 40,490 SRD patients (Table 1) to 471,6119 subjects dwelling in the Lazio Region, the second most populated region of Italy that includes the Rome metropolitan area. SRDs and comorbidity diagnoses were derived from the CReG classification while data on COVID-19 infection from a regional digital network. The risk was expressed as incidence rate ratio adjusted for demographics and comorbidities. We focused on the period from the 20th of February 2020 to the 31st of December 2020 to selectively assess a cohort of unvaccinated patients.

Table 2 reports peculiar patterns in terms of incidence, hospitalisation, intensive care unit (ICU) admission and death for the different SRDs. COVID-19 risk was increased in patients with Psoriatic Arthritis and Undifferentiated Connective Tissue Disease, possibly as the result of reduced adherence to protecting behaviours. These conditions are indeed less frequently treated with immunosuppressants or associated with visceral involvement, circumstances that have been reported to lead to highly perceived individual risk [4–6]. The hospitalization risk was higher in patients with Axial Spondylarthritis, Systemic Erythematosus Lupus (SLE), Systemic Vasculitis, intensive care unit (ICU) admission risk was higher in Systemic Erythematosus Lupus and primary Sjögren's syndrome patients, while increased mortality was reported in patients with Rheumatoid Arthritis, SLE, primary Sjögren Syndrome, and Scleroderma. It can be argued that the patients who are more likely to present pulmo-renal complications are more susceptible to worse outcomes. The high prevalence of lung fibrosis and the specific vasculopathy could explain the especially high mortality in scleroderma patients.

In conclusion, we showed how the CReG system classification allows the identification of high-risk SRD patients on a large scale

Table 1
Prevalence of SRDs in Lazio and demographics of the affected patients.

SRD diagnosis	Total patients, n	Prevalence, %	Overlapping SRDs, n (%)	Female, n (%)	Age 18–35, n (%)	Age 36–59, n (%)	Age 60–79, n (%)	Age ≥ 80, n (%)
RA	14838	0.31	1463 (9.86)	11581 (79.0)	1005 (0.10)	4755 (0.23)	7243 (0.58)	1835 (0.46)
PsA	11273	0.24	867 (7.72%)	6862 (61.0)	611 (0.06)	5192 (0.25)	4915 (0.40)	519 (0.13)
axSpA	2422	0.05	305 (12.59)	1118 (46.1)	255 (0.03)	1276 (0.06)	763 (0.06)	128 (0.03)
SLE	3936	0.08	682 (17.33)	3388 (86.0)	412 (0.04)	2261 (0.11)	1141 (0.09)	122 (0.03)
pSS	3393	0.07	989 (29.15)	3208 (94.5)	114 (0.01)	1324 (0.06)	1628 (0.13)	327 (0.08)
SSc	2256	0.05	522 (23.14)	2056 (91.1)	109 (0.01)	836 (0.04)	1107 (0.09)	204 (0.05)
MSD	952	0.02	296 (31.09)	797 (83.7)	83 (0.01)	418 (0.02)	405 (0.03)	46 (0.01)
UCTD	2977	0.06	695(23.25)	2745 (92.2)	386 (0.04)	1673 (0.08)	853 (0.07)	65 (0.02)
SV	1560	0.03	118 (7.56)	978 (62.6)	206 (0.02)	560 (0.03)	610 (0.05)	184 (0.05)

SRD: systemic rheumatic disease; SD: standard deviation; RA: rheumatoid arthritis; PsA: psoriatic arthritis; axSpA: axial spondylarthritis; SLE: systemic lupus erythematosus; pSS: primary Sjögren syndrome; SSc: systemic sclerosis; MSD: myositis-spectrum disorders; UCTD: undifferentiated connective tissue disease; SV: systemic vasculitis.

Table 2

Infection rates and thirty-day hospitalisation, ICU admission, and death rates in SRD patients with COVID-19.

Diagnosis	n	Tested patients, n (%)	Infection		Hospitalization		ICU admission		Death	
			Cases, n	Adjusted IRR (95% CI)	Cases, n	Adjusted IRR (95% CI)	Cases, n	Adjusted IRR (95% CI)	Cases, n	Adjusted IRR (95% CI)
RA	13375	3218 (24.06)	453	1.09 (0.99–1.19)	94	1.18 (0.96–1.45)	16	1.47 (0.90–2.41)	30	1.50[a] (1.04–2.17)
PsA	10370	2747 (26.49)	394	1.21[c] (1.10–1.33)	60	1.15 (0.89–1.48)	12	1.54 (0.87–2.72)	9	0.89 (0.46–1.73)
axSpA	2117	575 (27.16)	84	1.21 (0.98–1.50)	15	1.89[a] (1.14–3.14)	1	0.82 (0.12–5.82)	2	1.02 (0.25–4.12)
SLE	3254	908 (27.90)	128	1.14 (0.96–1.36)	24	2.16[c] (1.45–3.22)	5	3.67[b] (1.52–8.83)	5	2.67[a] (1.10–6.44)
pSS	2404	640 (26.62)	84	1.12 (0.90–1.38)	17	1.58 (0.98–2.54)	5	4.13[b] (1.71–9.96)	6	2.51[a] (1.12–5.62)
SSc	1734	528 (30.45)	46	0.84 (0.63–1.12)	10	1.23 (0.66–2.31)	0	–	6	4.60[c] (2.06–10.29)
MSD	656	170 (25.91)	22	1.03 (0.68–1.56)	4	1.78 (0.67–4.74)	0	–	0	–
UCTD	2282	726 (31.81)	95	1.26[a] (1.03–1.54)	10	1.45 (0.78–2.70)	0	–	0	–
SV	1442	409 (28.35)	53	0.99 (0.75–1.30)	14	1.81[a] (1.07–3.06)	2	1.33 (0.33–5.38)	4	2.31 (0.86–6.18)
Overlapping SRDs	2856	836 (29.27)	100	1.06 (0.87–1.28)	20	1.79[b] (1.16–2.78)	6	3.96[c] (1.78–8.84)	5	2.45[a] (1.02–5.91)
No SRDs	4675629	1054387 (22.55)	149092	1.00 (0.99–1.00)	17517	1.00 (0.98–1.02)	2570	0.99 (0.93–1.05)	3821	0.99 (0.92–1.08)
Lazio region	4716119	1065144 (22.59)	150551	–	17785	–	2617	–	3888	

SRD: systemic rheumatic disease; SD: standard deviation; RA: rheumatoid arthritis, PsA: psoriatic arthritis; axSpA: axial spondylarthritis; SLE: systemic lupus erythematosus; ICU: intensive care unit; pSS: primary Sjögren syndrome; SSc: systemic sclerosis; MSD: myositis-spectrum disorders; UCTD: undifferentiated connective tissue disease; SV: systemic vasculitis.

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] $P < 0.001$.

and highlights the heterogeneity in their clinical behaviours. This methodology could be fruitfully extended to the assessment of other potential SRD-related complications such as cancer and cardiovascular events

Funding

Disclosure of interest

The authors declare that they have no competing interest.

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