COVID-19 vaccine hesitancy in systemic sclerosis

Sirs,
Vaccine hesitancy is defined as the "delay in acceptance or refusal of vaccination despite availability of vaccination services" (1). The success of COVID-19 vaccination programs is a key determinant to abate the spread of the infection (2) and understanding what people feel might help to address hesitancy (3). Therefore, using the *"Oxford Covid-19 Vaccine Hesitancy Scale"* and *"Oxford COVID-19 Vaccine Confidence & Complacency Scale" (*4), we explored the attitudes towards COVID-19 vaccine in patients with systemic sclerosis (SSc) and which sociodemographic or disease-related factors might affect hesitancy. A control group of individuals affected by inflammatory arthritis was included.

Translation, linguistic validation and cultural adaptation of the two scales were performed according to the WHO best practice guidelines (https://www.who.int/substance_abuse/research_tools/translation/en/). On the basis of the responses, patients were categorised as "clearly positive", "very unsure" or "strongly hesitant" about COVID-19 vaccine. We included 104 patients with SSc and 111 controls. Characteristics of the study population are reported in Table I.

Seventy-five (72.1%) SSc and 96 (86.5%) arthritis patients had "clearly positive" feelings (*p*=0.009). Respectively, 16 (15.4%) and 6 (5.4%) patients were "very unsure" (*p*=0.016), while 3 (2.9%) and 5 (4.5%) had a "strongly hesitant" attitude (*p*=0.531).

In SSc patients, after stratification for median age [61.0 (50.25–59.0) years] and median disease duration [8.5 (4.0–15.0) years], we observed a significant difference in the hesitancy scale score in older *vs.* younger individuals (11.4±3.6 *vs.* 14.5±5.7, *p*<0.001, Fig 1A) but not in longer *versus* shorter disease duration (12.2±4.4 *vs.* 13.8±5.5, *p*=0.139, Fig 1B). Regarding cutaneous involvement, hesitancy scale score was lower in patients with higher mRSS (11.3±4.0 *vs.* 14.4±5.5, *p*=0.003, Fig 1C) and with diffuse *versus* limited disease subset (10.3±4.1 *vs.* 13.3±4.9, *p*=0.022, Fig 1D). Moreover, individuals with ILD were significantly less hesitant than patients with no ILD (11.6±4.5 *vs.* 14.3±5.3, *p*=0.012, Fig 1E) while no difference was retrieved according to treatment with immunosuppressive therapies or not (13.0±5.0 *vs.* 13.0±5.2, *p*=0.792, Fig 1F).

We found that the majority of SSc patients have positive attitudes towards COVID-19 vaccine. However, compared to inflammatory arthritis, less SSc patients have a strong intent to receive the vaccination, while a higher proportion is doubtful. Our data suggest that older individuals and patients with higher disease activity might

have more positive feelings about COVID-19 vaccine, similar to previous research outlining a lower vaccine hesitancy in people at higher risk of severe COVID-19 illness (4, 5). Interestingly, also the absence of differences based on ongoing immunosuppressive therapies is consistent with the available literature (6-8).

Campochiaro *et al.* found that 44% of patients with rheumatic diseases had a clear willingness to receive COVID-19 vaccine and an additional 37% answered positively when recommended by the caring rheumatologist (9). Boekel *et al.* showed that 61% of patients with autoimmune diseases accepted to receive vaccination against COV-
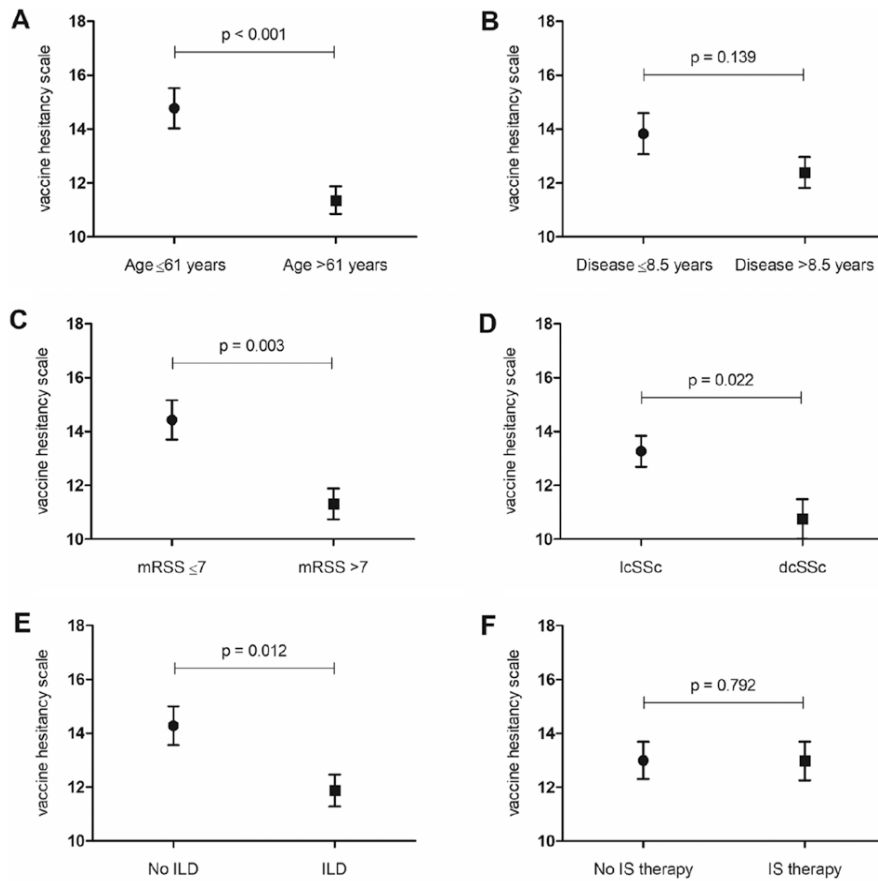
Table I. General characteristics of patients with systemic sclerosis and controls affected by inflammatory arthritis.

	Systemic sclerosis (n=104)	Inflammatory arthritis (n=111)	*p*-value
Socio-demographic characteristics			
Female, n (%)	90 (86.5)	66 (59.5)	<0.001
Age (years), mean (SD)	58.7 (12.9)	55.0 (15.8)	0.060
Age range 18-39 years, n (%)	9 (8.7)	20 (18.0)	0.450
Age range 40-54 years, n (%)	27 (26.0)	29 (26.1)	0.978
Age range 55-69 years, n (%)	48 (46.2)	42 (37.8)	0.217
Age range >69 years, n (%)	20 (19.2)	20 (18.0)	0.819
Employment status			
Employed	44 (42.3)	59 (53.2)	0.112
Homemaker	9 (8.7)	7 (6.3)	0.512
Unemployed	7 (6.7)	7 (6.3)	0.900
Retired	44 (42.3)	38 (34.2)	0.223
Highest level of education			
Middle school, n (%)	46 (44.2)	34 (30.6)	0.039
High school, n (%)	44 (42.3)	48 (43.2)	0.890
University, n (%)	14 (13.5)	29 (26.1)	0.020
Marital status			
Married, n (%)	69 (66.3)	69 (62.2)	0.523
Single, n (%)	22 (21.2)	26 (23.4)	0.690
Cohabiting, n (%)	10 (9.6)	10 (9.0)	0.878
Widowed, n (%)	3 (2.9)	6 (5.4)	0.356
Ever received influenza vaccination, n (%)	65 (62.5)	89 (80.2)	0.004
Ever received pneumococcal vaccination, n (%)	46 (44.2)	62 (55.9)	0.088
Had COVID-19	5 (4.8)	5 (4.5)	0.916
Disease characteristics and therapy			
Disease duration (years), mean (SD)	10.8 (8.3)	12.8 (9.5)	0.101
cDMARDs, n (%)	33 (31.7)	55 (49.5)	0.008
bDMARDs/tsDMARDs, n (%)	2 (1.9)	65 (58.6)	<0.001
Glucocorticoids, n (%)	35 (33.7)	20 (18.0)	0.009
Vasoactive therapy, n (%)	98 (94.2)		
Disease subset			
Limited cutaneous SSc, n (%)	71 (68.3)		
Diffuse cutaneous SSc, n (%)	25 (24.0)		
Sine scleroderma SSc, n (%)	8 (7.7)		
Rheumatoid arthritis, n (%)		51 (45.9)	
Psoriatic arthritis, n (%)		44 (39.6)	
Axial spondyloarthritis, n (%)		16 (14.4)	
Disease manifestations in SSc patients			
Interstitial lung disease, n (%)	51 (49.0)		
Digital ulcers, n (%)	58 (55.8)		
Pulmonary arterial hypertension, n (%)	4 (3.8)		
Gastrointestinal involvement, n (%)	29 (27.9)		
Oxford COVID-19 vaccine hesitancy scale score, mean (SD)	13.1 (4.9)	11.5 (4.6)	0.494
Oxford COVID-19 vaccine confidence & complacency scale score, mean (SD)	25.2 (6.9)	22.8 (6.0)	0.097
Attitude about COVID-19 vaccine			
Clearly positive, n (%)	75 (72.1)	96 (86.5)	0.009
Very unsure, n (%)	16 (15.4)	6 (5.4)	0.016
Strongly hesitant, n (%)	3 (2.9)	5 (4.5)	0.531
HADS-D, mean (SD)	9.0 (3.2)	9.2 (1.6)	0.184
HADS-A, mean (SD)	9.0 (3.3)	8.7 (2.5)	0.487
SF-36 MCS, mean (SD)	59.3 (21.2)	64.3 (23.3)	0.571
SF-36 PCS, mean (SD)	52.9 (24.3)	61.1 (25.1)	0.471

cDMARDs: conventional disease-modifying anti-rheumatic drugs; bDMARDs: biologic disease-modifying anti-rheumatic drugs; tsDMARDs: targeted synthetic disease-modifying anti-rheumatic drugs; SSc: systemic sclerosis; HADS-A: Hospital Anxiety and Depression Scale – Anxiety; HADS-D: Hospital Anxiety and Depression Scale – Depression; SF-36: Short Form-36.

Fig. 1. Oxford COVID-19 Vaccine Hesitancy Scale score after stratification for median age (**A**), median disease duration (**B**), median modified Rodnan skin score (mRSS) (**C**), diffuse cutaneous (dcSSc) or limited cutaneous (lcSSc) subsets (**D**), presence of interstitial lung disease (ILD) (**E**), use of immunosuppressive (IS) therapy (**F**).
Data are expressed as mean and standard error of the mean.

[1]Medicine & Rheumatology Unit, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy;
[2]Rheumatology Unit, School of Medicine, University of Modena and Reggio Emilia, Modena, Italy;
[3]Clinical Trial Center, Direzione Scientifica, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy;
[4]Department of Psychiatry, University of Oxford, Oxford, United Kingdom;
[5]Oxford Health NHS Foundation Trust, Oxford, UK;
[6]Scientific Direction, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy;
[7]Rheumatology Clinic Madonna dello Scoglio Cotronei, Crotone, Italy;
[8]Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Italy.

Please address correspondence to:
Jacopo Ciaffi,
Dipartimento di Medicina e Reumatologia,
IRCCS Istituto Ortopedico Rizzoli,
via Pupilli 1, 40136 Bologna, Italy.
E-mail: jacopo.ciaffi91@gmail.com

Competing interests: none declared.

© Copyright CLINICAL AND
EXPERIMENTAL RHEUMATOLOGY 2021.

ID-19 (7), while in the international survey "VAXICOV", Felten and colleagues described a proportion of 54% of rheumatology patients willing to receive COVID-19 vaccination (8).

Overall, in our survey clearly positive feelings towards COVID-19 vaccine are more frequent than previously reported. However, besides differences in the questionnaire structure, our survey was conducted after the approval in the European Union of the first three COVID-19 vaccines and it is conceivable that the authorisation positively affected perception about safety and effectiveness in the population.

In conclusion, our survey suggests that most patients with SSc have positive feelings towards COVID-19 vaccine, but uncertainties are present in a considerable proportion of cases. These results highlight the crucial role of the caring rheumatologists in addressing concerns and hesitancy of individuals affected by rheumatic diseases with the purpose of promoting vaccine literacy and enhancing vaccination rates.

J. CIAFFI[1], MD*
D. GIUGGIOLI[2], MD, PhD*
A. MARI[1]
M. D'ONGHIA[1]
A. SPINELLA[2], MD
V. BRUSI[1], MD
L. MANCARELLA[1], MD
L. LISI[1], MD
J. FARANDA CORDELLA[3], MD
D. FREEMAN[4,5], MD, PhD
M.P. LANDINI[6], MD
C. FERRI[2,7], MD
R. MELICONI[1,8], MD
F. URSINI[1,8], MD, PhD

*These authors contributed equally.

References

1. MACDONALD NE: Vaccine hesitancy: Definition, scope and determinants. *Vaccine* 2015; 33: 4161-4.
2. FLANAGAN KL, BEST E, CRAWFORD NW *et al.*: Progress and pitfalls in the quest for effective SARS-CoV-2 (COVID-19) vaccines. *Front Immunol* 2020; 11: 579250.
3. VERGER P, PERETTI-WATEL P: Understanding the determinants of acceptance of COVID-19 vaccines: a challenge in a fast-moving situation. *Lancet Public Health* 20; 6: e195-6.
4. FREEMAN D, LOE BS, CHADWICK A *et al.*: COVID-19 vaccine hesitancy in the UK: the Oxford coronavirus explanations, attitudes, and narratives survey (Oceans) II. *Psychol Med* 2020: 1-15.
5. MURPHY J, VALLIÈRES F, BENTALL RP *et al.*: Psychological characteristics associated with COVID-19 vaccine hesitancy and resistance in Ireland and the United Kingdom. *Nat Commun* 2021; 12: 29.
6. PRIORI R, PELLEGRINO G, COLAFRANCESCO S *et al.*: SARS-CoV-2 vaccine hesitancy among patients with rheumatic and musculoskeletal diseases: a message for rheumatologists. *Ann Rheum Dis* 2021; 80: 953-4.
7. BOEKEL L, HOOIJBERG F, VAN KEMPEN ZLE *et al.*: Perspective of patients with autoimmune diseases on COVID-19 vaccination. *Lancet Rheumatol* 2021; 3: e241-43.
8. FELTEN R, DUBOIS M, UGARTE-GIL MF *et al.*: Vaccination against COVID-19: Expectations and concerns of patients with autoimmune and rheumatic diseases. *Lancet Rheumatol* 2021; 3: e243-45.
9. CAMPOCHIARO C, TRIGNANI G, TOMELLERI A *et al.*: Potential acceptance of COVID-19 vaccine in rheumatological patients: a monocentric comparative survey. *Ann Rheum Dis* 2021 Jan 28 [Online ahead of print].