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# Experiences and Perceptions of People with Systemic Sclerosis with SARS-CoV-2 Vaccination: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Cross-sectional Study

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There is little information on COVID-19 vaccine safety in patients with autoimmune rheumatic diseases (ARDs), and patient concerns about possible adverse outcomes in ARDs contribute to vaccine hesitancy.[1-3] One study reported that people with systemic sclerosis (SSc) (N = 104) may be more hesitant than those with other ARDs (N = 111).[4] The only large study on vaccine experiences in ARDs (N = 2860) found that patient-reported adverse reactions were similar to the general population,[5] but results were not reported separately for SSc.

We surveyed participants in the international Scleroderma Patient-centered Intervention Network (SPIN) Cohort to evaluate (1) proportion vaccinated, (2) whether changes were made to medications pre-vaccination, (3) adverse reactions and associated factors, (4) degree of vaccine hesitancy, and (5) perceptions about factors potentially important to vaccination decisions.

Detailed methods are provided in Supplementary Material 1. The SPIN COVID-19 Patient Advisory Team was involved in survey development. The SPIN COVID-19 Vaccine Survey (Supplementary Material 2) was administered April 9 to May 15, 2021 in English and French via *Qualtrics*. SPIN Cohort[6] participants were invited to complete the survey via emails and popup invitations for those who completed routine cohort assessments during the study period. Responses were linked to sociodemographic and clinical data previously collected via the cohort. The study received ethics approval as an amendment to the SPIN Cohort study.

Participants indicated if they had received zero, one, or two COVID-19 vaccine dose, and those who had received a vaccination were asked about the brand, vaccination date, any medication adjustments made, and any adverse reactions experienced at each dose. Unvaccinated participants were asked how likely they were to be vaccinated using a 7-point Likert scale. Participants who reported they were unsure, more unlikely than likely, unlikely, or would certainly not get vaccinated were categorized as “hesitant”. All participants rated factors potentially important to vaccine decisions using a 5-point Likert scale. Multivariable logistic regression was conducted to assess associations of local (sore arm) and systemic reactions, separately, with age, sex, race/ethnicity, country, disease subtype, immunosuppressant use, vaccine brand, and history of COVID-19 infection.

Of 1,410 active SPIN Cohort participants, 1,000 consented, and 932 (66%) completed the full survey and were included in analyses. Supplemental Tables 1 and 2 show characteristics of survey respondents versus non-respondents and vaccinated versus unvaccinated participants. Among participants, 699 (75%) of 932 received at least one vaccine dose and 358 (38%) of 932 received two. Only 42 (6%) of 699 and 28 (8%) of 358 changed a medication prior to their first or second doses, respectively.

Adverse reactions were reported after the first and second dose by 270 (39%) of 699 and 209 (58%) of 358 participants, respectively (Table 1). The most common adverse reactions after first (N = 699) and second (N = 358) doses were sore arm (N = 211, 30%; N = 161, 45%), fatigue (N = 157, 23%; N = 143, 40%), and muscle ache (N = 60, 9%; N = 80, 22%). No severe reactions were reported. Worsening of at least one SSc symptom was reported after first and second doses by 41 (6%) and 28 (6%) participants, respectively. Variables independently associated with a systemic reaction (any reaction other than sore arm) after the first dose (Supplementary Table 3) included age in years (odds ratio 0.97, 95% confidence interval 0.96-0.99), male sex (0.36, 0.19-0.68), AstraZeneca vaccine (reference = Pfizer; 2.30, 1.37-3.84), and COVID-19 infection history (2.50, 1.32-4.72). For the second dose (Supplementary Table 4), there were independent associations with age (0.96, 0.94-0.98), male sex (0.36, 0.18-0.72), non-White race-ethnicity (0.49, 0.25-0.94), French participants (reference = United States; 0.41, 0.23-0.73), immunosuppressant use (0.60, 0.36-0.98) and Moderna vaccine (2.37, 1.34-4.18); only 21 participants received an Astra/Zeneca second dose.

Of 932 participants, there were 90 (10%) who were vaccine “hesitant”. Hesitancy was statistically significantly associated with younger age (mean 55 years versus 60 years for non-hesitant), country (France highest = 44 of 281 [16%] hesitant; United Kingdom lowest = 3 of 86 [3%]), current smoking (11 of 44 [25%]), and history of COVID-19 infection (16 of 77 [21%]). Hesitancy was greater among males and participants without interstitial lung disease or pulmonary hypertension, though not statistically significant (Supplementary Table 5). Compared to unvaccinated participants who planned to receive a vaccine, “hesitant” participants scored significantly higher on all 16 potential concerns including items related to COVID-19 vaccine effectiveness, the potential for adverse reactions, the vaccine development

process, and the need for COVID-19 vaccination (item scores 1-5; median difference in item means = 1.2 points; Supplementary Table 6).

For considerations in vaccine decision-making, the 842 (90%) of 932 participants who received or planned to receive the vaccine rated all 8 beliefs about vaccination (e.g., effectiveness, collaborative good, return to normal) significantly more important than hesitant participants (Supplementary Table 7). The greatest difference in ranking of important or very important was for vaccination being a civic duty (625 of 842, 74% versus 12 of 90, 13%; difference 61%, 95% CI 53-69%). When participants were queried regarding the importance of 10 information sources for decision making, the proportion rating important or very important was higher among non-hesitant participants for recommendations by their doctors (672 of 842, 80% versus 45 of 90, 50%; difference 30%, 19-40%) and the ability to discuss concerns with their doctor (626 of 842, 74% versus 56 of 90, 62%; difference 12%, 2-23%). Among hesitant patients, importance was higher for time to assess long-term negative effects (500 of 842, 60% versus 72 of 90, 80%; difference 20%, 12-30%) and experiences of other people with SSc with the vaccine (429 of 842, 51% versus 58 of 90, 64%; difference 13%, 3-24%).

In summary, 842 (90%) of 932 of respondents had been vaccinated by mid-May 2021 or intended to be vaccinated. Only 42 (6%) of 699 made medication changes prior to their first vaccination and 28 (8%) of 358 with the second. The proportion with adverse reactions was similar to the general population in clinical trials[7,8] and self-report in other ARDs.[5] Self-reported SSc flare was uncommon, and there were no serious adverse reactions. The proportion of vaccine hesitant participants was substantially lower than in general population studies,[9] which could relate to greater concern about infection among vulnerable people with SSc.

A strength of our study includes the high percentage of respondents from a large, multi-national cohort with similar participant characteristics to other major SSc cohorts.[10] Our study has several limitations. The SPIN Cohort is a convenience sample, and the subset of cohort participants who completed the SPIN COVID-19 Vaccine Survey may not be representative of all individuals with SSc; adverse reactions were self-reported, and opinions and degree of hesitancy may evolve with time.

This is the first, large study detailing COVID-19 vaccine experiences in SSc. Vaccination was safe in this group with no serious adverse events, a side effect profile similar to other populations, and a low rate of reported SSc flare.

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**Data Sharing:** De-identified individual participant data with a data dictionary and analysis codes that were used to generate the results reported in this article will be made available upon request to the corresponding author and presentation of a methodologically sound proposal that is approved by the Scleroderma Patient-centered Intervention Network Data Access and Publications Committee. Data will be available beginning 12 months after publication. Data requesters will need to sign a data transfer agreement.

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**Table 1. Self-reported adverse reactions following COVID-19 vaccination (N=699)**

| Adverse reaction, N (%) | First Dose (N=699) | Second Dose (N=358) |
|---|---|---|
| No adverse reaction | 429 (61%) | 149 (42%) |
| At least one adverse reaction[a] | 270 (39%) | 209 (58%) |
| Sore arm | 211 (30%) | 161 (45%) |
| Fatigue | 157 (23%) | 143 (40%) |
| Muscle ache | 60 (9%) | 80 (22%) |
| Joint pain | 42 (6%) | 41 (12%) |
| Flu-like symptoms | 46 (7%) | 50 (14%) |
| Fever | 42 (6%) | 49 (14%) |
| Chills | 42 (6%) | 59 (17%) |
| Shortness of breath | 15 (2%) | 9 (3%) |
| Rash | 13 (2%) | 10 (3%) |
| Severe allergy | 0 (0%) | 0 (0%) |
| Hives | 0 (0%) | 3 (1%) |
| At least one systemic sclerosis symptom worsening | 41[b] (6%) | 28[c] (6%) |

[a]Participants could report > 1 adverse reaction; [b]Most common systemic sclerosis symptoms worsening (first dose): fatigue (n=23), muscle weakness (n=13), shortness of breath (n=12), Raynaud's (n=11), arthritis (n=11); [c]Most common SSc symptoms worsening (second dose): fatigue (n=19), muscle weakness (n=11), gastrointestinal symptoms (n=11), arthritis (n=11), Raynaud's (n=8), shortness of breath (n=8).