Systemic rheumatic disease flares after SARS-CoV-2 vaccination among rheumatology outpatients in New York City

Vaccination against SARS-CoV-2 is crucial for patients with systemic rheumatic diseases (SRDs), who may be at increased risk of severe outcomes post-COVID-19.[1] However, as patients with SRDs were not included in the mRNA vaccine trials (ie, Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273)), no data exist regarding whether these vaccines might trigger SRD flares. Sparse data suggest that other vaccines may be associated with SRD flares,[2 3] possibly from molecular mimicry triggering immune activation or non-specific adjuvant effects. As SRD flares are associated with disease deterioration, increased flares could have serious clinical implications.[4]

We report the interim results of a web-based survey evaluating SRD flare incidence post-SARS-CoV-2 vaccine. The survey was e-mailed 5 March 2021 to 3545 outpatients with SRDs seen at a large rheumatology division in New York City. ICD-10 algorithms were used to identify SRDs (online supplemental material). A self-reported disease flare was defined as 'a sudden worsening of your rheumatology condition or arthritis' within 2 weeks of the vaccine.

As of 12 April 2021, out of 1483 respondents (41.8% response rate), 1101 patients (74.2%) with SRDs reported receiving at least one dose of a SARS-CoV-2 vaccine and provided flare data (mean age: 60.8 years (14.2 years); 80.6% female; 86.0% White and 5.7% Hispanic/Latinx ethnicity). Five hundred and ninety seven patients (54.2%) received Pfizer vaccine, 483 (43.9%) received Moderna vaccine, 16 (1.5%) received Janssen vaccine and 3 (0.3%) received AstraZeneca vaccine. A total of 202 SRD flares were reported by 165 patients (14.9%). History of suspected/confirmed COVID-19 occurred in 7.9% with SRD flare and 6.7% without SRD flare. Mean age of patients reporting an SRD flare was 59.6 years (13.9 years) versus 61.0 years (14.2 years) in the non-flare group; the majority of both groups were female (89.7% vs 80.0%), White (88.5% vs 85.6%) and non-Hispanic/Latinx (95.2% vs 92.2%). 15.9% of patients receiving Moderna vaccine and 14.2% receiving Pfizer vaccine reported SRD flares.

Of the patients receiving either Pfizer or Moderna vaccines, 654 (59.4%) had received both doses. Of these patients, 113 (17.0%) flared, 26 (23.0%) flared only after the first dose, 48 (42.5%) flared only after the second dose and 37 (32.7%) flared after both doses. Flares after the first and second dose of Pfizer vaccine were 10.3% vs 10.9%, and flares after the first and second dose of Moderna vaccine were 9.6% vs 16.3%, respectively.

Both the flare and non-flare groups used medications for prevention and treatment of vaccine side effects (table 1). Most SRD flares were characterised as moderate to severe (57.3% after first vs 62.4% after second dose), and as qualitatively 'typical' SRD flares (70.9% after first dose vs 68.2% after second dose). Flares were predominantly reported as joint pain, joint swelling,

Table 1 Vaccine and flare characteristics in outpatients with systemic rheumatic diseases, stratified by flare status post-COVID-19 vaccination

	First dose vaccine N=1101		Second dose vaccine* N=626	
	Flare N=117 (10.4%)	No Flare N=984 (87.5%)	Flare N=85 (13.6%)	No Flare N=541 (86.4%)
Vaccine manufacturer, N%				
Pfizer	67 (57.3%)	530 (53.9%)	35 (41.2%)	285 (52.7%)
Moderna	47 (40.2%)	436 (44.3%)	50 (58.8%)	256 (47.3%)
Janssen	3 (2.6%)	13 (1.3%)	N/A	N/A
AstraZeneca	0 (0%)	3 (0.3%)	0 (0%)	0 (0%)
Other†	0	1 (0.1%)	0	0
Missing	0	1 (0.1%)	0	0
Medications taken for prevention of COVID-19 vaccine side effects (prior to vaccine) (N, %)‡				
No medications	104 (88.9%)	911 (92.6%)	73 (85.9%)	502 (92.8%)
Benadryl	7 (6.0%)	20 (2.0%)	2 (2.4%)	13 (2.4%)
Corticosteroids	2 (1.7%)	7 (0.7%)	3 (3.5%)	4 (0.7%)
Acetaminophen	4 (3.4%)	29 (3.0%)	7 (8.2%)	24 (4.4%)
NSAIDs/CoX-2 inhibitors	4 (3.4%)	22 (2.2%)	1 (1.2%)	11 (2.0%)
Medications taken for treatment of COVID-19 vaccine side effects (after vaccine) (N, %)‡				
No medications	64 (54.7%)	748 (76.0%)	26 (30.6%)	310 (57.3%)
EpiPen	1 (0.9%)	0 (0%)	0 (0%)	0 (0%)
Benadryl	7 (6.0%)	10 (1.0%)	4 (4.7%)	13 (2.4%)
Corticosteroids	6 (5.1%)	3 (0.3%)	4 (4.7%)	5 (0.9%)
Acetaminophen	29 (24.8%)	152 (15.5%)	36 (42.4%)	166 (30.7%)
NSAIDs/CoX-2 inhibitors	25 (21.4%)	82 (8.3%)	31 (36.5%)	76 (14.1%)
Flare severity (N, %)				
Mild	50 (42.7%)		32 (37.7%)	
Moderate	49 (41.9%)		44 (51.8%)	
Severe	18 (15.4%)		9 (10.6%)	
Flare described as 'typical' (N, %)				
Yes	83 (70.9%)		58 (68.2%)	
No	18 (15.4%)		16 (18.8%)	
Not sure	16 (13.7%)		11 (12.9%)	
Flare symptoms (N, %)‡				
Fever	6 (5.1%)		9 (10.6%)	
Joint pain	98 (83.8%)		74 (87.1%)	
Joint swelling	56 (47.9%)		38 (44.7%)	
Skin rash	14 (12.0%)		10 (11.8%)	
Fatigue	62 (53.0%)		57 (67.1%)	
Muscle aches	57 (48.7%)		48 (56.5%)	
Other§	16 (13.7%)		11 (12.9%)	
Number of days after vaccine when flare started (N, %)				
1 day	30 (25.6%)		26 (30.6%)	
2–3 days	39 (33.3%)		26 (30.6%)	
4–7 days	35 (29.9%)		24 (28.2%)	
>7 days	13 (11.1%)		9 (10.6%)	
Length of flare (N, %)				
1 day	7 (6.0%)		2 (2.4%)	
2–4 days	23 (19.7%)		40 (47.1%)	
5–7 days	41 (35.0%)		16 (18.8%)	
8–21 days	28 (23.9%)		25 (29.4%)	
>21 days	18 (15.4%)		0 (0%)	
Missing	0		2 (2.4%)	

Flare defined as self-reported 'sudden worsening of rheumatology condition or arthritis' within 2 weeks of COVID-19 vaccination.
*654 patients reported receiving 2/2 vaccine doses, but 28 of these patients did not respond to second dose flare questions.
†One participant reported receiving Sinovac vaccine from China.
‡Rows not mutually exclusive.
§Other flare symptoms indicated by patients at first COVID-19 vaccine dose: paresthesias, swelling in face or feet, 'brain fog', muscle spasms, psoriasis rash, migraines. Other symptoms at second vaccine dose: paresthesias, swelling in face or feet, and muscle spasms.
CoX-2, cyclooxygenase-2; NSAIDs, nonsteroidal anti-inflammtory drugs.

muscle aches and fatigue (table 1). While 27.7% of flares started 1 day after vaccination, 61.4% began after 2–7 days and 10.9% occurred more than 7 days later (table 1). Most SRD flares resolved within 7 days of onset, but 26.2% lasted for 8–21 days and 8.9% for >21 days.

Interim data from our cohort demonstrate that >85% of patients did not report an SRD flare post-SARS-CoV-2 vaccination. This information is reassuring and can help inform vaccine decision-making for patients with SRDs. Although we did not collect laboratory studies, most SRD flares were described as 'typical', suggesting these symptoms are not vaccine's adverse effects being misreported as disease flares. However, when patients did flare, the majority of flares were reported as moderate to severe, with some lasting >3 weeks. Therefore, it will be important to follow these patients prospectively, as well as to perform analyses which incorporate potential confounders to identify predictors of SRD flares post-vaccination. Whether vaccine manufacturer is an independent predictor of SRD flare remains to be determined.

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