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Safety and tolerability of mRNA COVID-19 vaccines in people with antiphospholipid antibodies

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Vaccines represent a cornerstone in controlling the COVID-19 pandemic. The availability of data on the immunogenicity and safety of vaccines in patients with autoimmune diseases is progressively increasing.¹⁻³ However, some concerns have been raised regarding the safety of the vaccines in patients with antiphospholipid antibodies, as these antibodies have been reported to appear following both infection and vaccination and have been identified in patients with COVID-19.⁴ Although a few cases of thrombocytopenia and thrombotic events with clinical features resembling antiphospholipid syndrome have been reported in recipients of adenoviral vector-based or mRNA-based COVID-19 vaccines,⁵ a pathogenic link and, more critically, the clinical relevance of antiphospholipid antibodies in these clinical settings have yet to be fully elucidated.

To assess the safety and tolerability of COVID-19 vaccines in people with antiphospholipid antibodies, we surveyed 102 vaccinated patients at the Center of Research of Immunopathology and Rare Diseases (San Giovanni Bosco Hub Hospital, Turin, Italy), of whom 52 had a diagnosis of antiphospholipid syndrome and 50 have antiphospholipid antibodies without clinical features of the syndrome (table). 67 (66%) of 102 patients received the Comirnaty BNT162b2 mRNA (tozinameran, Pfizer-BioNTech) vaccine and 35 (34%) received the Spikevax mRNA 1273 (elasomeran, Moderna) vaccine. 89 (87%) participants had received two doses of vaccine and 13 (13%) had received a single dose of vaccine because of a previous PCR-proven SARS-CoV-2 infection. The study was reviewed and approved by Comitato Etico Interaziendale Città Di Torino. Participants provided written informed consent to participate in this study.

78 (76%) of 102 patients had at least one side-effect: 45 (44%) reported pain at the injection site, 37 (36%) fatigue, and 29 (28%) headache. Symptoms were transient and self-limiting within 10 days. There were no differences in frequencies of systemic side-effects between the two mRNA vaccines. Symptoms were reported as mild in 72 (71%) patients and moderate in 30 (29%). No symptoms compatible with new thrombotic events were reported. The rate of reactions was not different when comparing those after the first and second doses. Only one patient with thrombotic antiphospholipid syndrome and a known history of mild thrombocytopenia ($110\,000/\text{mm}^3$), who was on long-term vitamin K antagonist therapy, reported the occurrence of self-limiting purpuric lesions on her calves 10 days after the second dose. Blood tests were unremarkable except for a single transient fluctuation of platelet count ($88\,000/\text{mm}^3$). Consequent

investigations (during an observation time of 5 months) showed a platelet count persistently above $100\,000/\text{mm}^3$.

Although more data are needed, including from long-term follow-up, immunogenicity data from our survey show that mRNA COVID-19 vaccines seem to have an acceptable safety and tolerability profile in patients with antiphospholipid antibodies. No major adverse effects nor thrombotic events were reported. Side-effects seem frequent, but mild and transient in nature.

We declare no competing interests.

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	Surveyed patients (n=102)
Age (years)	52 (18-77)
Female	87 (85%)
Male	15 (15%)
Antiphospholipid antibody carrier	50 (49%)
Antiphospholipid syndrome	52 (51%)
Primary antiphospholipid syndrome	38 (37%)
Antiphospholipid syndrome associated to SLE	14 (14%)
Thrombotic antiphospholipid syndrome	42 (41%)
Obstetric antiphospholipid syndrome	10 (10%)
Antiphospholipid antibody profile	
Lupus anticoagulants	77 (76%)
Anticardiolipin antibodies (IgG/IgM)	67 (66%)
Anti- β 2-glycoprotein 1 antibodies (IgG/IgM)	56 (55%)

Data are n (%) or median (range). SLE=systemic lupus erythematosus.

Table: Demographic and clinical characteristics of surveyed patients