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COVID-19: Clinical features and outcomes in unvaccinated 2-dose and 3-dose vaccinated against SARS-CoV-2 patients with systemic autoimmune and autoinflammatory rheumatic diseases

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ABSTRACT

Clinical data on vaccinated patients with coronavirus disease 2019 (COVID-19) who have systemic autoimmune and autoinflammatory rheumatic diseases (SAARD) are limited. This observational study aimed to report the clinical features and outcomes of COVID-19 among cases with SAARD that were unvaccinated or were 2- and 3-dose vaccinated against SARS-CoV-2 and were consecutively recorded by the treating physician. Unvaccinated and 2- and 3-dose vaccinated patients were compared in terms of COVID-19 symptomatology, hospitalizations, oxygen supplementation requirements, and death rates. From the beginning of the pandemic to February 15, 2022, 134 vaccine-naïve COVID-19 cases were recorded among our study cohort. From March 1, 2021 to February 15, 2022, 89 2-dose vaccinated and 105 3-dose vaccinated patients who were infected with SARS-CoV-2 $\geq$14 days after the second dose were included. The hospitalization rate was higher in the unvaccinated (n = 36, 26.9%) than in the 2-dose (n = 13, 14.6%, p = 0.03) or 3-dose (n = 5, 4.8%, p < 0.001) vaccinated patients. Severe/critical COVID-19 cases requiring oxygen supplementation were the least among 3-dose vaccinated (n = 4, 3.8%) compared to both 2-dose vaccinated (n = 12, 13.5%, p = 0.018) and unvaccinated (n = 25, 18.7%, p < 0.001) patients. ICU admission and death rates were similar among unvaccinated (n = 5, 3.7% and n = 3, 2.2%, respectively) and 2-dose vaccinated patients (n = 4, 4.5%; and n = 2, 2.2%, respectively), while no 3-dose vaccinated patients died or required ICU admission. Logistic regression analysis revealed a significant inverse association between 3-dose vaccination and severe/critical COVID-19 (OR = 0.078, 95% CI: 0.022–0.273, p < 0.001). In conclusion, these findings argue in favor of booster vaccination against SARS-CoV-2 in patients with SAARD.

1. Introduction

Systemic autoimmune and autoinflammatory rheumatic diseases (SAARD) comprise a group of chronic disorders of unknown etiology that share the following two common characteristics: (i) over-reactivity of the immune system towards self-tissues and organs and (ii) chronic therapy with conventional and targeted immunosuppressive and immunomodulatory agents. These two elementary factors play an essential role in the observed predisposition of such patients to infections; therefore, vaccination against infectious agents, particularly SARS-CoV-2, is of paramount importance [1]. However, immunosuppressive treatments often hamper vaccine immunogenicity, as shown in previous studies [2–5]. Regarding the vaccinations against COVID-19, which have spanned for more than 14 months, concerns have been raised on the risk of SARS-CoV-2 infection among fully vaccinated individuals with SAARD, since mutated virus strains have arisen and

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vaccine-elicited immunity has been shown to decline over time [6–10]. Furthermore, it remains unclear whether vaccinated patients with SAARD are at a higher risk of adverse outcomes related to breakthrough SARS-CoV-2 infection. Preliminary data show that breakthrough COVID-19 may occur in vaccinated patients with SAARD, occasionally leading to hospitalization and death [11–14]. Nevertheless, the outcomes seem to be better than those in unvaccinated patients. In this study, we present a comparative analysis of the clinical features and outcomes of COVID-19 among unvaccinated and 2- and 3-dose vaccinated patients with SAARD, which highlights the importance of booster vaccination in such patients.

2. Materials and methods

2.1. Patients and methods

Since the beginning of the COVID-19 vaccination campaign in Greece, patients with SAARD were followed up in the rheumatology outpatient clinics of the Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens, Department of Physiology, School of Medicine, National and Kapodistrian University of Athens, Department of Rheumatology, Faculty of Medicine, School of Health Sciences, University of Ioannina, and the Department of Medicine and Clinical Immunology, Euroclinic of Athens in Greece, and among them cases with document SARS-CoV-2 infection following COVID-19 vaccination consecutively recorded. Patients aged <16 years, those infected with SARS-CoV-2 in <14 days after the second vaccine dose, and those treated for COVID-19 with oral antivirals or monoclonal antibodies were excluded. Data were recorded by the treating physician using a structured questionnaire with the following components: (i) demographic characteristics (age and sex) and comorbidities (arterial hypertension, cardiovascular disease, diabetes, dyslipidemia, and chronic lung disease including lung involvement related to the underlying SAARD), (ii) SAARD-related characteristics (disease type and disease activity based on physician's global assessment [remission or minimal/low vs. moderate or severe/high disease activity] as previously reported [15] and immunosuppressive/immunomodulatory treatment regimens), (iii) COVID-19 vaccination-related details (vaccine type and number and dates of doses administered), and (iv) COVID-19-related characteristics (date of infection confirmed by PCR or viral antigen testing on the nasopharyngeal swab material, symptomatology, and COVID-19-related severity and outcomes). Demographic data, comorbidities, and SAARD-related characteristics were extracted from the patients' medical records by the treating physician. The severity of SARS-CoV-2 infection was classified according to the National Institutes of Health COVID-19 Treatment Guidelines [16].

To investigate the potential effect of immunization against SARS-CoV-2 on COVID-19 severity and outcomes, we compared vaccinated and unvaccinated cases with SAARD that had COVID-19 and had been consecutively recorded since the beginning of the pandemic, a portion of which has been previously described [17].

This study complies with the principles of the Declaration of Helsinki and the General Data Protection Regulation of the European Union and was approved by the ethics committees of the affiliated participating centers. All patients provided written informed consent prior to participation in the study.

2.2. Statistical analysis

Descriptive characteristics are expressed as median and range (minimum–maximum) or frequencies and percentages. Analyses of categorical data between groups were performed using the chi-square test or Fischer's exact and Fischer-Freeman-Halton tests when cell counts were ≤5. For continuous variables, normality was tested with the Shapiro–Wilk test, and subsequently either the Mann–Whitney test or *t*-test was applied where appropriate. The statistical significance level was set at a p-value ≤ 0.05. Factors associated with severe/critical COVID-19 in the univariate analyses ($p < 0.05$) were introduced into a multivariable logistic regression model to estimate the independent association between vaccination status and COVID-19 severity. Hospitalization and death were not evaluated as outcomes of interest because hospitalizations might have been influenced by many factors (e.g., variable thresholds for hospital admission) during the various phases of the pandemic and the number of recorded deaths was low, respectively. Statistical analysis was performed using SPSS V. 21.0 (IBM Corp., Armonk, N.Y., USA).

3. Results

Since the beginning of the pandemic (March 2020) and up to February 15, 2022, 134 vaccine-naive COVID-19 positive patients with SAARD were identified. Between March 1, 2021 and February 15, 2022, 202 vaccinated cases with SAARD infected with SARS-CoV-2 were consecutively recorded. Among them, five patients who were infected before completion of the recommended 2-dose vaccination schedule or within 14 days after the second dose [11], and three patients who had been treated with molnupiravir or monoclonal antibodies against the virus were excluded. Therefore, 194 vaccinated patients with breakthrough infections were included for further analysis. Majority of the vaccinated patients (n = 181, 93.3%) had initially received an mRNA-based SARS-CoV-2 vaccine (either BNT162b2; Pfizer/BioNTech or mRNA-1273; Moderna), whereas the rest (n = 13, 6.7%) had been vaccinated with the adenovirus-based vaccine (ChAdOx1 nCoV-19; AstraZeneca). Among the vaccinated patients, 89 (45.9%) had received two doses and 105 (54.1%) had received three doses (2-doses in the context of the initial vaccination schedule plus an mRNA-based booster dose [BNT162b2; Pfizer/BioNTech] at ≥3 months after the second dose). The median time intervals between the last SARS-CoV-2 vaccine dose and COVID-19 diagnosis were 165 (14–295) and 63 (2–186) days for those vaccinated with two and three doses, respectively (Supplementary Figure 1).

Most of the patients included in the study were females (n = 230, 70.1%), and the median (range) age was 50 (17–91) years. More than half of the patients (n = 185, 56.4%) had systemic vasculitis or connective tissue diseases, including systemic lupus erythematosus, antiphospholipid syndrome, Sjögren's syndrome, systemic sclerosis, inflammatory myopathies, and mixed or undifferentiated connective tissue diseases. Inflammatory arthritis, including rheumatoid arthritis, seronegative spondyloarthritis, and juvenile idiopathic arthritis, was the second most common type of disease (n = 125, 38.1%), while other immune-mediated diseases (retroperitoneal fibrosis, Still's disease, relapsing polychondritis, and periodic fever syndromes) were recorded in 18 patients (5.5%). Unvaccinated and 2- and 3-dose vaccinated patients with SAARD did not differ in terms of demographics, type of SAARD, and comorbidities. Regarding therapeutic regimens, there were fewer patients without immunosuppressive/immunomodulatory treatments (off-treatment) in the "3-dose vaccinated" group (n = 4, 3.8%) compared to the "unvaccinated" group (n = 19, 14.2%, p = 0.014), while no differences were found between the other group comparisons. Furthermore, 3-dose vaccinated individuals (n = 58, 55.2%) compared to unvaccinated individuals (n = 50, 37.3%) were more commonly treated with corticosteroids (CS) (p = 0.006) and 2-dose vaccinated (n = 11, 12.4%) compared to unvaccinated individuals (n = 4, 3%, p = 0.011) were more frequently treated with rituximab (RTX) (Supplementary Table 1).

The differences in the reported symptomatology are shown in Table 1. More specifically, 3-dose vaccinated patients with SAARD patients experienced fever, anosmia, and loss of taste less frequently (n = 57, 54.3%; n = 4, 3.8%; and n = 5, 4.8%, respectively) than those experienced by both 2-dose vaccinated (n = 66, 74.2%, p = 0.005; n = 17, 19.1%, p < 0.001; and n = 19, 21.3%, p < 0.001, respectively) and unvaccinated patients (n = 101, 75.4%, p < 0.001; n = 33, 24.6%, p < 0.001; and n = 25, 18.7%, p = 0.001, respectively). Similarly, 3-dose

Table 1
COVID-19 symptomatology, severity, and outcomes.

	Unvaccinated patients (n = 134)	2-dose vaccinated patients (n = 89)	3-dose vaccinated patients (n = 105)	p-value[a]
Symptomatology				
Fever, n (%)	101 (75.4)	66 (74.2)	57 (54.3)	<0.001
Cough, n (%)	54 (40.3)	45 (50.6)	44 (41.9)	0.291
Shortness of breath, n (%)	23 (17.2)	8 (9)	5 (4.8)	0.007
Fatigue, n (%)	69 (51.5)	45 (50.6)	38 (36.2)	0.040
Headache, n (%)	38 (28.4)	25 (28.1)	31 (29.5)	0.971
Nasal congestion/rhinorrhea, n (%)	19 (14.2)	36 (40.4)	52 (49.5)	<0.001
Sore throat, n (%)	25 (18.7)	14 (15.7)	38 (36.2)	<0.001
Diarrhea, n (%)	28 (20.9)	5 (5.6)	9 (8.6)	0.001
Arthralgias, n (%)	19 (14.2)	18 (20.2)	13 (12.4)	0.288
Myalgias, n (%)	36 (26.9)	19 (21.3)	17 (16.2)	0.139
Anosmia, n (%)	33 (24.6)	17 (19.1)	4 (3.8)	<0.001
Loss of taste, n (%)	25 (18.7)	19 (21.3)	5 (4.8)	<0.001
Vomiting, n (%)	6 (4.5)	1 (1.1)	1 (1)	0.224
Rash, n (%)	2 (1.5)	1 (1.1)	0 (0)	0.625
Cognitive dysfunction, n (%)	2 (1.5)	0 (0)	0 (0)	0.341
Seizures, n (%)	1 (0.7)	0 (0)	0 (0)	1.000
SARS-CoV-2 severity classification				
Asymptomatic/mild/moderate, n (%)	109 (81.3)	77 (86.5)	101 (96.2)	0.001
Severe/critical, n (%)	25 (18.7)	12 (13.5)	4 (3.8)	
COVID-19-related outcomes				
Hospitalization, n (%)	36 (26.9)	13 (14.6)	5 (4.8)	<0.001
Hypoxygonemia, n (%)	25 (18.7)	12 (13.5)	4 (3.8)	0.001
ICU admission, n (%)	5 (3.7)	4 (4.5)	0 (0)	0.067
Death, n (%)	3 (2.2)	2 (2.2)	0 (0)	0.277

[a] Comparison among the three groups.

vaccinated patients with SAARD reported nasal congestion/rhinorrhea and sore throat (n = 52, 49.5%; n = 38, 36.2%) more frequently than those reported by unvaccinated patients (n = 19, 14.2%, p < 0.001; and n = 25, 18.7%, p = 0.002). In contrast, unvaccinated patients with SAARD experienced diarrhea more frequently (n = 28, 20.9%) than that experienced by both 2-dose (n = 5, 5.6%, p = 0.002) and 3-dose vaccinated patients (n = 9, 8.6%, p = 0.009).

The hospitalization rate was higher in the unvaccinated group (n = 36, 26.9%) than in the 2-dose (n = 13, 14.6%, p = 0.03) or 3-dose (n = 5, 4.8%, p < 0.001) vaccinated groups. Similarly, severe/critical COVID-19 cases with hypoxemia were less frequently observed among the 3-dose vaccinated (n = 4, 3.8%) compared to both 2-dose vaccinated (n = 12, 13.5%, p = 0.018) and unvaccinated patients (n = 25, 18.7%, p < 0.001). Only few unvaccinated (n = 5, 3.7; and n = 3, 2.2%, respectively) and 2-dose vaccinated patients with SAARD (n = 4, 4.5%; and 2, 2.2%, respectively) died or required intensive care unit (ICU) admission, while no triple vaccinated patient died or required ICU admission or died (Table 1, Fig. 1). The characteristics of the patients who died are summarized in Table 2.

Unvaccinated patients with severe/critical COVID-19 (experiencing hypoxemia) compared to their unvaccinated counterparts with asymptomatic, mild, or moderate illness, were significantly older (median age,

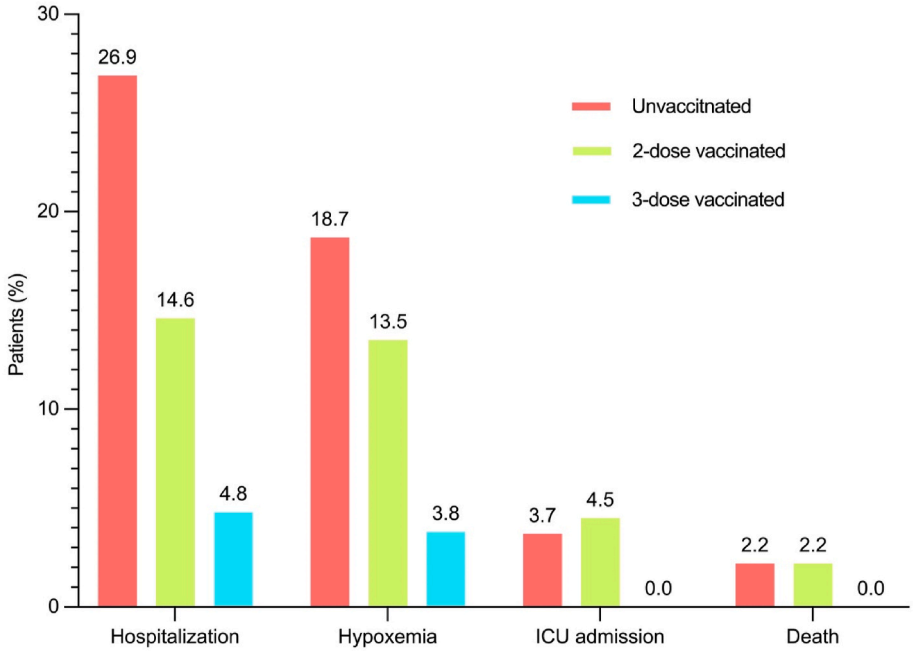

Fig. 1. Covid-19-related outcomes according to vaccination status.

Table 2
Characteristics of deceased patients with SAARD.

Sex (Age)	SAARD (activity)	Treatment	Comorbidities	Symptoms	SARS-CoV-2 vaccination details	Time period between vaccination and infection
			Vaccinated			
Female (84)	SS (low)	Prednisone 2.5 mg/day, Hydroxychloroquine	Hypertension, Cardiovascular disease, Chronic lung disease, Obesity	Fever, Shortness of breath	2-dose mRNA	211 days (before Omicron variant arrival in Greece)
Male (74)	IMM (low)	Prednisone 2.5 mg/day, Mycophenolate mofetil, Rituximab	Hypertension Diabetes Mellitus Chronic lung disease	Fever, Cough	2-dose mRNA	128 days (before Omicron variant arrival in Greece)
			Unvaccinated			
Male (57)	RA (low)	Prednisone 10 mg/day, Mycophenolate mofetil, Rituximab	Chronic lung disease, Obesity	Fever, Shortness of breath	N/A	N/A (before Omicron variant arrival in Greece)
Female (54)	SSc (moderate)	Prednisone 5 mg/day, Mycophenolate mofetil	Chronic lung disease, Obesity	Fever, Shortness of breath	N/A	N/A (before Omicron variant arrival in Greece)
Male (44)	SLE (high)	Prednisone 5 mg/day, Mycophenolate mofetil, Rituximab	Cardiovascular disease, Chronic lung disease, Obesity	Fever, Cough, Shortness of breath	N/A	N/A (before Omicron variant arrival in Greece)

SAARD, systemic autoimmune and autoinflammatory rheumatic disease; SS, Sjogren's syndrome; IMM, idiopathic inflammatory myopathy; RA, rheumatoid arthritis; SSc, systemic sclerosis; SLE, systemic lupus erythematosus.

57 vs. 47; $p < 0.001$), were more frequently diagnosed with systemic vasculitides (16% vs. 3.7%, $p = 0.04$), had more frequent chronic lung disease (45.8% vs. 11.9%, $p < 0.001$), and were more commonly treated with CS (56% vs. 33%, $p = 0.032$), mycophenolate mofetil (MMF) (32% vs. 7.3%, $p < 0.001$), and RTX (12% vs. 0.9%, $p = 0.021$) (Supplementary Table 2). The multivariable analysis showed that older age (OR = 1.074, 95% CI: 1.034–1.116, $p < 0.001$) and treatment with MMF (OR = 5.926, 95% CI: 1.613–21.774, $p = 0.007$) were potential independent predictors of severe/critical disease. Similarly, vaccinated patients with severe/critical COVID-19 compared to vaccinated patients with asymptomatic, mild, or moderate COVID-19 were significantly older (median age, 66 vs. 50, $p < 0.001$), were more frequently diagnosed with inflammatory myopathies (18.8% vs. 2%, $p = 0.013$) with high SAARD activity (43.8% vs. 8.4%, $p < 0.001$), had more frequent chronic lung disease (62.5% vs. 16.9%, $p < 0.001$), arterial hypertension (50% vs. 18%, $p = 0.002$), and obesity (17.1% vs. 7.7%, $p = 0.009$), and were treated with CS (81.3% vs. 47.2%, $p = 0.016$) and RTX (31.3% vs. 7.3%, $p = 0.009$) (Supplementary Table 2). In the multivariable analysis, moderate or high SAARD activity (OR = 5.737, 95% CI: 2.230–28.963, $p = 0.001$), chronic lung disease (OR = 6.620, 95% CI: 2.051–21.372, $p = 0.002$), and obesity (OR = 5.860, 95% CI: 1.479–23.224, $p = 0.012$) were independently associated with hypoxemia. Similar results were obtained when the vaccinated patients were stratified by the number of doses administered to them (Supplementary Table 3). No consistent pattern between different SAARDs and severe/critical COVID-19 was observed (Supplementary Table 4). Notably, 8 of 16 (50%) unvaccinated patients treated with MMF and 3 of 4 (75%) unvaccinated patients treated with RTX in the previous year developed severe/critical COVID-19. Moreover, less than half of the 2-dose vaccinated patients treated with MMF (n = 4/11, 36.6%) and RTX (n = 5/11, 45.5%) developed severe/critical disease. In contrast, only 1 of the 19 3-dose vaccinated patients who received MMF, and none of the 7 patients treated with RTX progressed to severe/critical COVID-19.

The multivariable analysis of all the patients with SAARD identified 3-dose vaccination status as significant independent protective factor against severe COVID-19 (OR = 0.078, 95% CI: 0.022–0.273, $p < 0.001$) when accounting for SAARD activity, presence of comorbidities and treatments with CS, MMF, and RTX; while increasing age (OR = 1.054, 95% CI: 1.021–1.088, $p = 0.001$) and SAARD activity (OR = 2.841, 95% CI: 1.042–7.746, $p = 0.041$) were associated with more severe COVID-19 course (Supplementary Tables 5 and 6).

One case of reinfection was observed in a 41-year-old female patient with inflammatory arthritis treated with low-dose prednisone (2.5 mg/day) and weekly methotrexate. The patient's first infection with SARS-CoV-2 was 15 days after her 2-dose mRNA vaccination schedule in September 2021, and the second infection was in February 2022. During the initial breakthrough infection, she presented with fever and myalgia while during the reinfection, she presented with only cough; both episodes were mild courses without complications. Two patients with periodic fever syndromes experienced a disease flare during SARS-CoV-2 infection (one 3-dose vaccinated patient with familial mediterranean fever and one unvaccinated patient with tumor necrosis factor receptor-associated periodic syndrome), and their symptomatology completely subsided following an increase in colchicine dose.

4. Discussion

In the current study, we present the clinical spectrum of COVID-19 in a cohort of patients with SAARD, according to vaccination status against SARS-CoV-2. Older age, high burden of comorbidities, and inadequately controlled SAARD necessitating intense immunosuppressive therapies are well-recognized risk factors for poorer clinical outcomes in patients with SAARDs infected with SARS-CoV-2 [15,18,19]. Our results reemphasize our previous findings regarding risk factors for severe/critical COVID-19 disease among patients with SAARD [17], while any differences in rates of hospitalization and severe/critical COVID-19 course might be attributed to the inclusion of additional patients with moderate/high SAARD activity that delayed COVID-19 vaccination as per recommendations [20,21] and COVID-19 cases infected in later time periods when the Delta variant was the predominant circulating variant in Greece [6,22].

Vaccinated patients with SAARD with breakthrough COVID-19 had better outcomes in terms of hospitalization and oxygen supplementation requirements than that had by unvaccinated patients; in particular, these outcomes were significantly better among 3-dose vaccinated compared to 2-dose vaccinated and unvaccinated patients with SAARD.

Among the patients in this study, vaccinated patients who had received their third vaccination dose experienced more frequent upper respiratory symptoms and less frequent olfactory and generalized symptoms related to COVID-19. This result is somewhat expected due to the initiation of the booster vaccination campaign for immunosuppressed patients and the concurrent spread of the omicron variant in Greece [22].

Importantly, deceased patients were older, had chronic lung disease,

and were treated with CS, MMF, or RTX, which are associated with worse COVID-19 clinical outcomes [15,17,19] and blunted humoral responses to SARS-CoV-2 vaccination [2–4]. In addition, deceased patients were infected during the pre-omicron era, and both vaccinated patients were infected with SARS-CoV-2 before receiving the booster vaccine dose.

Only a few studies have investigated and described the clinical characteristics and outcomes of patients with SAARD infected with SARS-CoV-2 [11–13]. Hospitalization and death rates among vaccinated patients with SAARD in our cohort were lower than those reported by Lawson-Tovey et al. and Cook et al. who reported the need for hospitalization and reported the occurrence of death in up to 38% and 20% of cases, respectively [12,13]. These reports, however, present only a few cases, and the differences can be attributed to the sample size, study period, and diverse patient characteristics between the cohorts. Notably, COVID-19-related outcomes in this study were similar to the findings of a registry-based study performed in Greece by the Greek Rheumatology Society [11] that showed that approximately 10% of 2-dose vaccinated patients were hospitalized with oxygen supplementation requirements and that no deaths were observed.

Our study has some limitations. First, selection bias cannot be excluded since asymptomatic or very mild COVID-19 cases might have been missed. Second, most unvaccinated patients were infected in an earlier time period (before the introduction of COVID-19 vaccines). This could presumably reflect different circulating SARS-CoV-2 variants and other undisclosed characteristics between the groups, such as behaviors of patients and physicians' management strategies during the various phases of the COVID-19 pandemic. Thus, the lack of difference in ICU admissions or deaths between unvaccinated and 2-dose vaccinated patients could be partially attributed to the explanation above. In addition, the fact that vaccinated patients were more frequently treated with CS and RTX than that observed in their unvaccinated counterparts might reflect the tendency of patients receiving certain immunosuppressants (which have been associated with adverse outcomes) to be immunized to be protected from COVID-19. Third, the number of patients who were admitted to the ICU or who died was low; therefore, conclusions regarding ICU admissions and mortality should be interpreted with caution. However, the fact that no ICU admission or death was observed in 3-dose vaccinated patients is encouraging. Fourth, data on immune responses after vaccination were not available for all patients to draw definitive conclusions.

In conclusion, 3-dose vaccinated patients with SAARD, compared to unvaccinated or 2-dose vaccinated patients, are protected from severe breakthrough SARS-CoV-2 infections. Further studies are needed to assess the risk of breakthrough infections and the efficacy of immunization among vaccinated patients with SAARD.

Authors' contributions statement

Athanasios-Dimitrios Bakasis: Resources, Data curation, Methodology, Software, Formal analysis, Writing – original draft, Writing – review & editing, Conceptualization, Final Approval. Clio P. Mavragani: Resources, Data curation, Methodology, Software, Formal analysis, Writing – original draft, Writing – review & editing, Conceptualization, Final Approval. Paraskevi V. Voulgari: Resources, Methodology, Writing – review & editing, Final Approval. Nafsika Gerolymatou: Resources, Data curation, Writing – review & editing, Final Approval. Ourania D. Argyropoulou: Resources, Writing – review & editing, Final Approval; Panayiotis G. Vlachoyiannopoulos: Resources, Methodology, Writing – review & editing, Final Approval. Fotini N. Skopouli: Resources, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Conceptualization, Supervision, Final Approval. Athanasios G. Tzioufas: Resources, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Conceptualization, Supervision, Final Approval. Haralampos M. Moutsopoulos: Resources, Data curation, Methodology, Writing – review & editing, Conceptualization, Supervision, Project administration, Final Approval.

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Declarations of competing interest

None.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaut.2022.102846.

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