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ORIGINAL RESEARCH

Risk of new-onset polymyalgia rheumatica following COVID-19 vaccination in South Korea: a self-controlled case-series study

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ABSTRACT

Background While several studies have reported some cases of polymyalgia rheumatica (PMR) following COVID-19 vaccination, studies using large databases are lacking.

Objectives To investigate the risk of PMR after COVID-19 vaccination using self-controlled case series (SCCS) analysis

Methods We used the National Health Insurance Database, linked with the COVID-19 registry between February 2021 and August 2023, to identify adults aged 50 years or older who received at least one dose of COVID-19 vaccine and subsequently diagnosed with PMR within the observation period, defined as 240 days after the first dose of vaccine. The risk window was defined as 28 days after each dose of COVID-19 vaccination, and the control window encompassed the remainder of the observation period. Incidence rate ratios (IRRs) were estimated using conditional Poisson regression with 95% CIs, stratified by dose and vaccine type.

Results Among 44 818 078 COVID-19 vaccine recipients, 376 patients were diagnosed with PMR. The analysis indicated that COVID-19 vaccination was not associated with an increased risk of PMR (IRR, 0.74; 95% CI 0.59 to 0.94). Rather, the risk of PMR was slightly reduced after the first dose (0.52; 0.34 to 0.79), with no significant association with other doses of COVID-19 vaccine (0.83; 0.59 to 1.16 for second dose, 0.77, 0.48 to 1.25 for third dose).

Conclusion In this nationwide SCCS, there was no association with the increased risk of PMR following COVID-19 vaccination. While these findings support the safety of COVID-19 vaccines, interpretation of the decreased risk of PMR should be cautious.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ While several case reports have suggested a plausible association between COVID-19 vaccination and polymyalgia rheumatica (PMR), few studies used large databases.

WHAT THIS STUDY ADDS

⇒ In this nationwide real-world study, we found no association between COVID-19 vaccination and an increased risk of PMR, regardless of vaccine dose or type.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings provide reassurance about the safety of COVID-19 vaccines, particularly in populations at risk of rheumatic diseases such as PMR.

INTRODUCTION

Since the beginning of the COVID-19 pandemic, over 13.3 billion doses of vaccines against SARS-CoV-2 have been administered.[1] In South Korea, approximately 88% of the population has received at least one dose of the COVID-19 vaccine through the national immunisation programme in August 2022,[2] which has prevented death and postsequelae from COVID-19.[3 4] However, despite the efforts to develop safe vaccines, large-scale vaccination inevitably led to the incidences of unexpected and very rare adverse events. Therefore, adverse events of special interest (AESIs) have been defined as concerns that require ongoing active vaccine safety surveillance,[5] and these systems have rapidly detected potential safety signals.[6 7]

Polymyalgia rheumatica (PMR), an immune-mediated inflammatory disorder causing stiffness and pain in muscles and affecting people over the age of 50,[8 9] could also be considered an AESI. Notably, several case reports of patients experiencing PMR after the administration of COVID-19 vaccines have been reported, and further research is needed to identify the potential association.[10 11] Increased activation of toll-like receptor 7 (TLR7) has been considered a plausible mechanism of PMR that might be induced by COVID-19 vaccines, although

this remains unclear.[11] Moreover, safety signals for PMR have been detected through analyses using VigiBase, the WHO global database of individual case safety report.[12–14] These findings have identified PMR as the most common postvaccination symptom in the category of inflammatory rheumatic diseases, suggesting a potential risk of PMR using the reporting OR. However, there is a lack of research using large databases to investigate the risks of COVID-19 vaccination, including whether the incidence of adverse events varies by dose and type of vaccine.

To address this evidence gap, this study aimed to evaluate the risk of PMR following COVID-19 vaccination in South Korea using self-controlled case series (SCCS) analysis.

METHOD

Data source

This study was part of the COVID-19 Vaccine Safety Research Committee (CoVaSC) in South Korea, which aimed to generate evidence for the safe use of COVID-19 vaccines. CoVaSC used a large-linked database, linking COVID-19 immunisation registry provided by the Korea Disease Control and Prevention Agency (KDCA) with health insurance claims data from the National Health Information Database (NHID).[15]

The COVID-19 immunisation registry includes COVID-19 vaccination information, such as vaccine type, date and dosing schedule as well as COVID-19 infection confirmed by PCR or rapid antigen test during the pandemic of COVID-19. The NHID covers all reimbursable healthcare services, representing approximately 98% of the entire population in South Korea.[16] The NHID contains anonymised identifiers of individuals with comprehensive information on demographic characteristics (eg, age, sex and type of health insurance), medical records such as diagnoses, treatments, procedures, drug prescriptions (eg, generic name, quantity, duration and route of administration of drug) and date of death. Diagnoses are recorded according to the International Classification of Diseases, 10th Revision (ICD-10), and prescriptions of drugs are recorded according to the National Drug Codes, mapping to the Anatomical Therapeutic Chemical classification.

This study was approved by the Public Institutional Review Board Designated by the Ministry of Health and Welfare (P01-202203-01-005) and the Institutional Review Board (IRB) of Sungkyunkwan University (SKKU 2024-08-006). Informed consent was not required since this study was conducted using anonymised claims data.

Study population

As PMR is rarely seen in people under the age of 50,[17 18] we identified individuals aged 50 years and older who received the first dose of COVID-19 vaccine between 26 February 2021 and 31 August 2023. Among these individuals, those with a diagnosis code for PMR were included in this SCCS analysis. We excluded individuals who were foreigners as those registered as foreign residents in South Korea, those vaccinated outside of South Korea and those with invalid vaccination records to avoid potential exposure misclassification. To meet the SCCS design assumptions that the outcome should not influence subsequent exposures and that the outcome should be an independent event in recurrence, we restricted the study population to those diagnosed with new-onset PMR after COVID-19 vaccination.[19] We excluded those with a history of PMR within 1 year prior to the date of first diagnosis of PMR after COVID-19 vaccination. We also excluded patients diagnosed with PMR after 240 days from the date of their first dose of the COVID-19 vaccine, which was considered to be the period when vaccine effectiveness is thought to persist.[20 21] The flowchart of the selection of study participants is outlined in figure 1.

SCCS analysis

To evaluate the risk of PMR after COVID-19 vaccination, we used the SCCS analysis.[19 22] This analysis includes patients who experienced both exposure and outcomes during the study period and compares the occurrence of outcomes in the risk window, which is the period defined as potentially relevant to the exposure, and the control window, which is the period outside the risk window. This design was adopted to investigate the safety of COVID-19 vaccines, due to high rates of vaccination in the South Korean population, making it difficult to select a control group. As each individual serves as their own control, time-invariant covariates such as demographics, genetic factors and previous clinical conditions are inherently controlled.[23]

The observation period was defined as the 240-day period following the first dose of COVID-19 vaccine (online supplemental material 1). The duration of the risk window was defined as the period up to 28 days after each dose, based on previous case reports[12 14] and the clinical trial, which indicated that neutralising antibodies against SARS-CoV-2 peaked 28 days after vaccination.[24] The control window encompassed the remaining days within the observation period.

COVID-19 vaccination and PMR

Any dose of COVID-19 vaccine during the study period was defined as an exposure and included the following vaccine types: mRNA-1273, BNT162b2, ChAdOx1/nCoV-19, Ad26.COV2.S and NVX-CoV2373. Other vaccines require two doses for completion of primary series, whereas a single dose of Ad26.COV2.S is considered as completion. Therefore, the risk of PMR was assessed by the number of vaccine doses to identify differences in immunisation and by the type of vaccine to evaluate the differences in biological mechanisms of action.

Outcomes

The outcome of interest was defined as the presence of a diagnosis code of PMR (ICD-10: M35.3) in the primary or secondary diagnosis position on either inpatient or

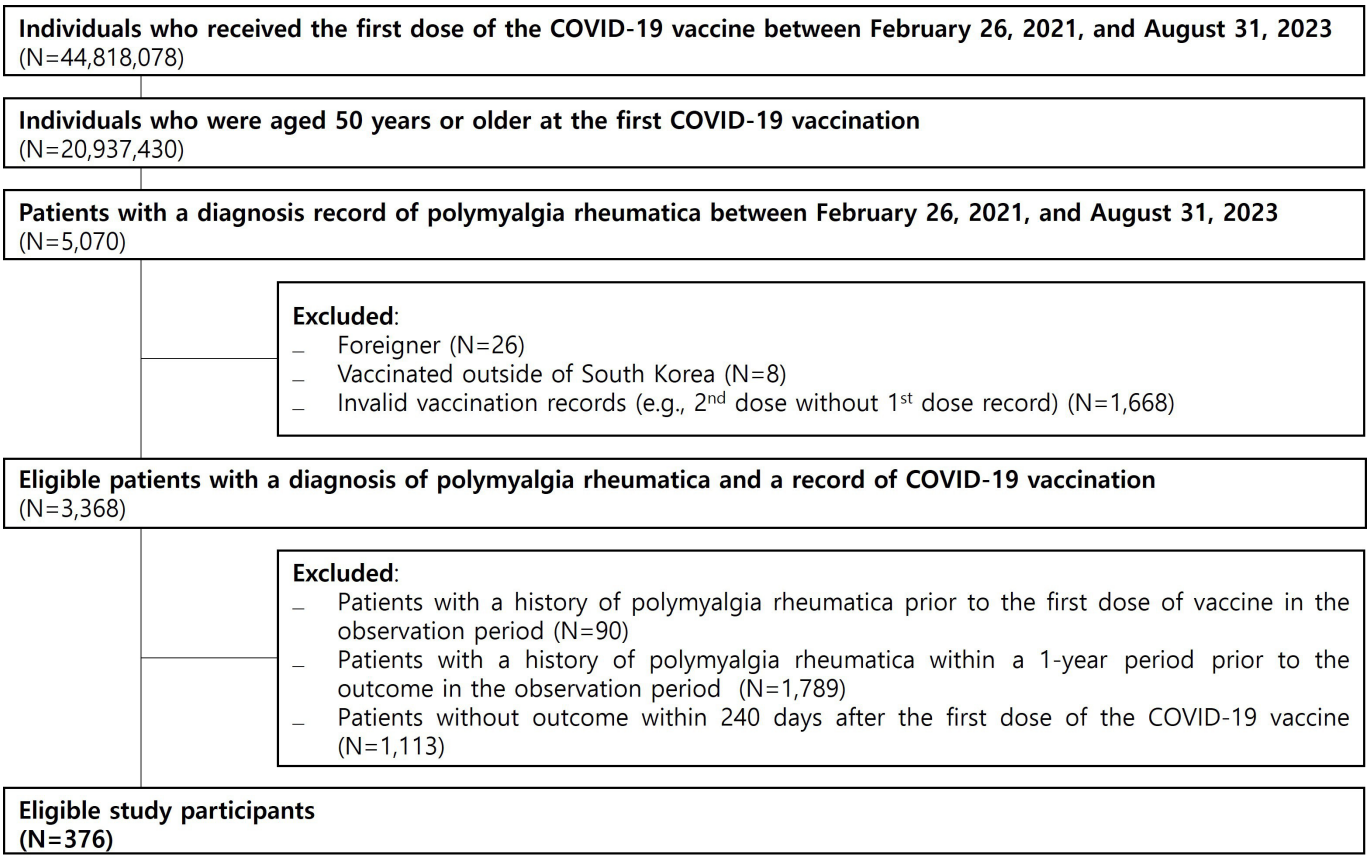

Figure 1 Flowchart of the study participant selection.

outpatient visits. To enhance the validity of the outcome, rare and interactive disease (RID) codes (V139) were considered to be present on the same day as the diagnosis of PMR. The definition of PMR was decided through review by the CoVaSc Clinical Research Committee. The outcome was defined by considering only the first occurrence to avoid violating the assumptions of the SCCS analysis that outcomes must be independently recurrent or rare.[19]

Statistical analysis

Baseline characteristics of PMR cases were assessed using the linked data for 1 year prior to the first COVID-19 vaccination and were presented using means and SDs for continuous variables and frequencies with percentages for categorical variables, categorised by the occurrence of PMR in the risk or control window. Demographic characteristics were measured by 10-year age group, sex, type of health insurance and region of residence at the date of the first COVID-19 vaccination. Clinical characteristics were measured by including comorbidities such as peripheral vascular disease, chronic lung disease, peptic ulcer disease and diabetes mellitus as well as the Charlson Comorbidity Index (CCI) within 1 year prior to the first COVID-19 vaccination. Detailed definitions of comorbidities are provided in online supplemental material 2. Differences in these baseline characteristics were assessed using t-tests for continuous variables and χ^2 tests for categorical variables, with a p value of less than 0.05 considered statistically significant.

For the primary analysis, the number of events and person-years were measured to estimate the incidence rate of PMR in the risk and control windows. Based on the SCCS analysis, conditional Poisson regression analyses were used to assess the risk of PMR after COVID-19 vaccination by estimating incidence rate ratios (IRRs) and 95% CIs. We performed the analyses stratified by scheduled dose (first, second and third). For secondary analyses, we conducted analyses stratified by the type of vaccine (mRNA-1273, BNT162b2, ChAdOx1/nCoV-19, Ad26.COV2.S and NVX-CoV2373). Subgroup analyses were also performed stratified by age (50–59, 60–69, 70–79, over 80 years), sex (male, female), health insurance type (national health insurance, medical aid), region of residence (metropolitan, rural), CCI (<5, 5+) and history of each comorbidity.

To further test the robustness of our findings, we performed several sensitivity analyses. First, we repeated our primary analysis by modifying the duration of the risk window (14, 42 and 60 days) to test the potential impact of the length of the risk window. Second, we excluded patients who were infected with COVID-19 during the observation period to consider the impact of COVID-19 on PMR. Third, we adjusted COVID-19 infection and seasonality as a time-varying confounder. Finally, we

redefined PMR using only diagnosis codes to address the potential misclassification of outcomes.

RESULT

Of the 44 818 078 individuals who received a COVID-19 vaccine between 26 February 2021 and 31 August 2023, there were 20 937 430 individuals who were aged 50 years or older, and we have identified 376 patients who developed PMR after COVID-19 vaccination who were included in the SCCS analysis (figure 1).

In the analysis, there were 87 patients with new-onset PMR identified in the risk window, with a mean age of 68.4 years (SD, 8.4) and 32.2% male. Among patients with new-onset PMR in the control window, we identified 289 patients with a mean age of 68.5 years (SD, 9.5) and 27.3% male (table 1). Except for the history of renal

Table 1 Baseline characteristics of polymyalgia rheumatica cases administered with COVID-19 vaccines, stratified by exposure windows

	Risk window		Control window		
	N	%	N	%	P value
Total	**87**	**100**	**289**	**100.0**	
Age, years (mean, SD)	68.4	8.4	68.5	9.5	0.94
50–59	12	13.8	51	17.6	0.34
60–69	35	40.2	111	38.4	
70–79	31	35.6	81	28.0	
80+	9	10.3	46	15.9	
Sex					
Male	28	32.2	79	27.3	0.38
Female	59	67.8	210	72.7	
Health insurance type					
National health insurance	87	100.0	279	96.5	0.08
Medical aid	0	0	10	3.5	
Region of residence					
Metropolitan	64	73.6	193	66.8	0.23
Rural	23	26.4	96	33.2	
Comorbidities					
CCI (mean, SD)	2.8	2.2	2.5	2.1	0.23
CCI<5	71	81.6	242	83.7	0.64
CCI≥5	16	18.4	47	16.3	
Myocardial infarction	0	0.0	4	1.4	0.27
Congestive heart failure	4	4.6	28	9.7	0.14
Peripheral vascular disease	18	20.7	65	22.5	0.72
Cerebrovascular disease	12	13.8	52	18.0	0.36
Dementia	4	4.6	28	9.7	0.14
Chronic pulmonary disease	22	25.3	67	23.2	0.69
Rheumatic disease	32	36.8	79	27.3	0.09
Peptic ulcer disease	29	33.3	85	29.4	0.49
Mild liver disease	26	29.9	103	35.6	0.32
Serious liver disease	0	0	1	0.3	0.58
Diabetes mellitus	36	41.4	93	32.2	0.11
Renal disease	9	10.3	13	4.5	0.04
Cancer	9	10.3	18	6.2	0.19
HIV infection	0	0	0	0	–

CCI, Charlson Comorbidity Index Score; COVID-19, Coronavirus infectious disease 2019; HIV, Human Immunodeficiency Virus; SD, Standard Deviations .

	No. of Event		Person-Years		IR*		IRR (95% CI)	Forest plot
	Risk	Control	Risk	Control	Risk	Control		
Overall	87	289	70.67	174.25	1.23	1.66	0.74 (0.59-0.94)	
Scheduled dose								
1st dose	23	289	26.81	174.25	0.86	1.66	0.52 (0.34-0.79)	
2nd dose	38	223	27.08	131.32	1.40	1.70	0.83 (0.59-1.16)	
3rd dose	26	38	16.73	18.82	1.55	2.02	0.77 (0.48-1.25)	
Vaccine type								
BNT162b2	35	126	29.83	75.41	1.17	1.67	0.70 (0.49-1.02)	
mRNA-1273	3	19	4.14	9.93	0.73	1.91	0.38 (0.12-1.23)	
ChAdOx1-S	6	61	9.20	34.75	0.65	1.76	0.37 (0.16-0.84)	
Ad26.COV2.S	0	1	0.08	0.58	0.00	1.72	-	
NVX-CoV2373	0	1	0.08	0.36	0.00	2.79	-	

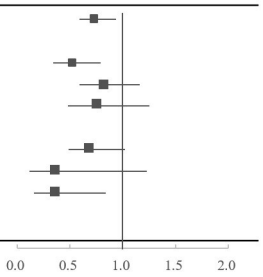

Figure 2 Risk of new-onset polymyalgia rheumatica following COVID-19 vaccinations, overall and stratified by scheduled doses and type of vaccine. IRR, incidence rate ratio. *Per-person year.

disease (10.3% patients in the risk window, 4.5% in the control window), there were no significant differences observed between the two groups, as the p value was greater than 0.05 in most covariates. During the observation period, five patients died, along with one patient in the risk window and four patients in the control window.

Overall, the incidence rate of PMR was 1.23 per one person-year in the risk window and 1.66 per one person-year in the control window, and there was decreased risk of PMR in the first 28 days after any dose of COVID-19 vaccine (IRR, 0.74; 95% CI 0.59 to 0.94). When stratified by the scheduled dose of COVID-19 vaccine, a decreased risk of PMR was identified for the first dose (0.52; 0.34 to 0.79), but no significant association between the risk of PMR and vaccine was observed for the second (0.83; 0.59 to 1.16) and third doses (0.77; 0.48 to 1.25). When stratified by vaccine type, mRNA vaccines were not associated with an increased risk of PMR (0.70; 0.49 to 1.02 for BNT162b2; 0.38; 0.12 to 1.23 for mRNA-1273), and there was a decreased risk of PMR within 28 days after COVID-19 administration with ChAdOx1-S (0.37; 0.16 to 0.84) (figure 2).

In subgroup analyses by age, a decreased risk was observed in patients who were 50–59 years old (0.53; 0.29 to 0.98), and no risk was observed in age groups over 60 years. Furthermore, in subgroup analyses stratified by gender, insurance type, region, CCI and comorbidities, most of the results all indicated no increased risk of PMR after COVID-19 vaccination (table 2). Also, sensitivity analyses of varying the length of the risk window, modifications to the outcome definition and addressing COVID-19 infection showed results consistent with the main findings (online supplemental material 3 and 4).

DISCUSSION

In this nationwide real-world study from South Korea, we found no association between the risk of new-onset PMR and COVID-19 vaccination. Also, no associations with the risk of PMR were found in the analysis of all COVID-19 vaccine doses and types. In fact, a decreased risk of PMR was observed in the first dose of combined analysis of all COVID-19 vaccine types and combined doses of ChAdOx1-S analysis. Subgroup and sensitive analyses by varying the age groups, sex, insurance type, region, comorbidities and risk window were consistent with the main findings. While interpretation of the decreased risk of PMR should be cautious, these findings support the evidence for the safety of COVID-19 vaccines against PMR.

This study was part of the CoVaSC project, which aimed to provide evidence for the safe use of COVID-19 vaccines. Some reports of PMR following COVID-19 vaccination have highlighted the need for a study to assess the risk of PMR.[12 13 25] However, there have been limited studies evaluating the association between PMR and COVID-19 vaccines using large databases, with only a few pharmacovigilance studies. Previous pharmacovigilance studies in France and South Korea reported an increase in PMR cases in patients receiving COVID-19 vaccines compared with those receiving all other medications or vaccines.[12 13] However, in the analysis where the comparator was limited to the influenza vaccine, PMR was not observed as a potential safety signal. These studies highlighted that, while there was an increased reporting of PMR following COVID-19 vaccination, this risk did not appear significant when compared specifically to influenza vaccines.[25] This suggests that the association between COVID-19 vaccines and PMR might be overstated when broader medication categories are used as comparators. These results had limitations due to difficulty in selecting proper comparison groups given the discordant results in different comparison groups and the possibility of information bias and selective reporting.[26] In addition, most adverse events in pharmacovigilance studies were reported from non-Asian countries, including the USA and Europe, and several studies suggested a lower incidence of PMR in Asian populations compared with other ethnic groups.[8 27 28] This suggested that ethnic differences should be considered. Therefore, we conducted the SCCS study using a nationwide database to assess the risk of COVID-19 vaccines and concluded that there was no association with the risk of PMR after vaccination.

The mechanisms of PMR associated with the COVID-19 vaccination are still not fully understood. Some studies have suggested that the inflammatory properties of the vaccine adjuvants may activate the immune system and induce inflammatory manifestations, leading to a development of a disease such as PMR.[25 29 30] Other studies have also suggested that possible polymorphisms in immune-mediated genes

Table 2 Subgroup analyses on the risk of new-onset polymyalgia rheumatica following COVID-19 vaccinations, stratified on age, sex, insurance type, region, CCI and comorbidities

	Number of events		Person-years		IR*		
	Risk	Control	Risk	Control	Risk	Control	IRR (95% CI)
Age, years							
50–59	12	51	12.32	27.81	0.97	1.83	0.53 (0.29 to 0.98)
60–69	35	111	27.79	68.27	1.26	1.63	0.77 (0.54 to 1.11)
70–79	31	81	20.91	52.25	1.48	1.55	0.96 (0.64 to 1.43)
80+	9	46	9.65	25.92	0.93	1.77	0.53 (0.26 to 1.07)
Sex							
Male	28	79	19.72	49.71	1.42	1.59	0.89 (0.59 to 1.36)
Female	59	210	50.95	124.54	1.16	1.69	0.69 (0.52 to 0.91)
Health insurance type							
National health insurance	87	279	68.71	169.90	1.27	1.64	0.77 (0.61 to 0.97)
Medical aid	0	10	1.96	4.35	0.00	2.30	–
Region of residence							
Metropolitan	64	193	48.54	118.83	1.32	1.62	0.81 (0.62 to 1.07)
Rural	23	96	22.12	55.42	1.04	1.73	0.60 (0.39 to 0.94)
CCI							
CCI<5	71	242	58.32	145.33	1.22	1.67	0.73 (0.57 to 0.94)
CCI≥5	16	47	12.34	28.92	1.30	1.63	0.80 (0.45 to 1.41)
Comorbidities							
Myocardial infarction	0	4	0.85	1.92	0.00	2.08	–
Congestive heart failure	4	28	5.53	14.82	0.72	1.89	0.38 (0.14 to 1.05)
Peripheral vascular disease	18	65	15.45	38.67	1.17	1.68	0.69 (0.42 to 1.16)
Cerebrovascular disease	12	52	11.40	30.27	1.05	1.72	0.61 (0.33 to 1.14)
Dementia	4	28	5.97	14.91	0.67	1.88	0.36 (0.13 to 1.00)
Chronic pulmonary disease	22	67	17.17	40.39	1.28	1.66	0.77 (0.48 to 1.23)
Rheumatic disease	32	79	22.63	49.41	1.41	1.60	0.88 (0.59 to 1.32)
Peptic ulcer disease	29	85	21.74	52.21	1.33	1.63	0.82 (0.55 to 1.23)
Mild liver disease	26	103	24.61	59.17	1.06	1.74	0.61 (0.40 to 0.92)
Serious liver disease	0	1	0.23	0.42	0.00	2.37	–
Diabetes mellitus	36	93	24.86	59.17	1.45	1.57	0.92 (0.63 to 1.34)
Renal disease	9	13	4.35	10.16	2.07	1.28	1.62 (0.71 to 3.68)
Cancer	9	18	5.53	12.21	1.63	1.47	1.10 (0.49 to 2.50)

*Per person-year.
CCI, Charlson comorbidity index; CI, Confidence interval; IR, incidence rate; IRR, incidence rate ratio.

may affect in development of PMR.[31] Also, the activation of the immune system through mechanisms such as TLR stimulation has been believed to play a role in triggering the inflammatory cascade that can lead to PMR in genetically susceptible individuals.[8 27] Furthermore, cytokine release, particularly interleukin-6, has been implicated in the inflammatory response associated with PMR.[8 27 29] While the hypotheses of these studies may be a plausible explanation of the risk of PMR following COVID-19 vaccination, our study using the real-world data did not demonstrate any association between the risk of PMR and COVID-19 vaccination. However, the findings of a decreased risk of PMR after vaccination in this study should be interpreted with caution. Interpreting these findings, it would be important to consider a healthy vaccinee effect, which refers to a situation where individuals who decide to vaccinate would be generally healthier than those who decline vaccination and may be less likely to experience PMR during the risk window.[32] In addition, adverse events such as muscle and joint pain, which commonly occurred after COVID-19 vaccination, were similar to PMR symptoms and may have masked PMR that occurred during the risk window, possibly leading to underestimated outcomes.

Furthermore, several previous studies indicated that COVID-19 infection significantly increased the risk of rheumatic diseases, including PMR.[33–35] Considering that the immunisation confers protection against COVID-19 infection, COVID-19 vaccination subsequently may also reduce the risk of PMR triggered by COVID-19 infection.[14 36 37] Therefore, given our findings, vaccination may be a feasible strategy to mitigate the risk of PMR during the COVID-19 pandemic.

This study has several strengths. First, to the best of our knowledge, this is the first large population cohort study conducted to investigate the risk of PMR following COVID-19 vaccination using large real-world data. Second, KDCA has mandated the collection of all COVID-19 vaccination and infection cases in South Korea, and since our database used a registry provided by KDCA, the definition of COVID-19 vaccination and infection is highly sensitive. Also, linking this registry to the NHID, which contains the nationwide claims data, allowed us to obtain robust findings. Finally, the SCCS analysis enabled us to avoid bias caused by comparing vaccinated and unvaccinated individuals in a population with high rates of COVID-19 vaccination and effectively controlled for time-invariant confounders.

This study has several limitations. First, the potential for misclassification and incomplete capture of the recorded outcomes could not be ruled out. To minimise this potential, PMR cases were captured with the combined uses of the ICD and RID codes. However, PMR symptoms such as muscle and joint pain might have been under-reported or misdiagnosed, especially during the risk window following vaccination, as these symptoms overlap with common postvaccination side effects. Second, there might be a delay between the actual disease onset and diagnosis recorded in the database. The median time from symptom onset to PMR following COVID-19 vaccination was reported to be 10 days in a national survey conducted.[25] Meanwhile, the mean duration of PMR symptoms before diagnosis was estimated to be 8.1±8.6 months.[38] This may have impacted our study findings. Nevertheless, the results of sensitivity analysis by varying the length of the risk windows were consistent with the main results. Third, the true incidence of postvaccination PMR may be underestimated due to a lack of awareness of PMR in clinical practice.[39] Fourth, although our study provides important insights into the relationship between COVID-19 vaccination and PMR, it is limited by the lack of detailed clinical information on each patient, including laboratory data or genetic factors that could influence the development of PMR. This highlights the need for further research incorporating more granular clinical and genetic data to better understand the pathophysiology behind vaccination-induced PMR. Also, due to a lack of information on other kinds of vaccines, such as influenza vaccines, we were limited to consider concomitant vaccination with COVID-19 vaccines. This highlighted the need for further research on the safety of COVID-19 vaccines when concomitantly given with other kinds of vaccines. Fifth, our study included subjects aged over 50 years, therefore, it is unclear whether the findings of the study could be generalised to younger men and women. Sixth, the data on the socioeconomic status of patients, which may have an impact on access to healthcare services and subsequently on treatment, were not included in this study. Finally, subgroup analyses were conducted stratifying by demographic characteristics such as sex, age, insurance type and comorbidities. However, due to the small sample size, some results could not be presented, which highlights the need for further research with a larger population to obtain more robust results. We expected that the treatments provided by the Korean healthcare system would not differ between individuals, as the NHID included only those individuals who are covered by the Korean healthcare system.

CONCLUSION

In this nationwide SCCS study using a large-linked database, there was no association with an increased risk of PMR after COVID-19 vaccination, whether by vaccine dose or type. In terms of clinical implications, our findings suggest that COVID-19 vaccination is safe concerning the risk of developing PMR. This could help inform clinical guidelines, reassuring healthcare providers and patients about the safety of vaccination, particularly in populations at risk of rheumatic diseases like PMR. However, clinicians should remain vigilant for potential symptoms of PMR, especially in patients with predisposing factors or those who report persistent musculoskeletal symptoms postvaccination.

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Contributors J-YS had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design; acquisition, analysis, or interpretation of data; administrative, technical, or material support; acquisition, analysis, or interpretation of data; critical revision of the manuscript for important intellectual content: all authors. Drafting of the manuscript: JW, MKK, HL. Statistical analysis: JW. Supervision: J-YS, H-AK. J-YS is the guarantor.

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Patient consent for publication Not applicable.

Ethics approval Ethical approval was obtained from the Public Institutional Review Board (IRB) Designated by Ministry of Health and Welfare (P01-202203-01-005) and the IRB of Sungkyunkwan University (SKKU 2024-08-006). This study

adhered to the ethical principles outlined in the Declaration of Helsinki. Given the utilisation of anonymised claims data in this study, the requirement for informed consent was waived.

Provenance and peer review Not commissioned; externally peer-reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Data for this study are provided by the Korea Disease Control and Prevention Agency and the National Health Insurance Service. Although legal data sharing agreements prohibit disclosure of the data, permission to access the data can be obtained through the submission of a well-defined request that includes explicit details on the required data, analysis methodology and plans for dissemination. Such requests should be directed to the Korea Disease Control and Prevention Agency and the National Health Insurance Service.

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