COVID-19



Safety of SARS-CoV-2 vaccines in patients with myasthenia gravis: a meta-analysis

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To the Editor:

We read with interest a recent article reported by Trinchillo A. in this journal [1], which found that COVID-19 vaccines were safe in myasthenia gravis (MG) patients. MG is an autoimmune disease affecting the neuromuscular junction, which can involve the ocular, respiratory, and skeletal muscles of the limbs. MG patients are predisposed to develop respiratory diseases in more severe forms due to muscular weakness. The COVID-19 vaccines have been shown to prevent severe COVID-19 in vulnerable patients. However, worsening MG induced by the COVID-19 vaccine has been seen in a few studies [2, 3]. Therefore, a meta-analysis of the safety of COVID-19 vaccination in MG patients is of significant importance.

Qian Zheng, Yongran Cheng, and Chengxin Song contributed to the work equally and should be regarded as co-first authors.

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We searched the EMBASE, Web of Science, and Pub-Med databases from January 1, 2020, to April 20, 2023, using the following keywords: COVID-19 vaccines, SARS-CoV-2 vaccines, 2019-nCoV vaccine, and myasthenia gravis. We restricted the search language to English. Studies were selected based on the following inclusion criteria: MG patients who received SARS-CoV-2 vaccines and English articles. Exclusion criteria were (1) studies without relevant data and (2) repeated studies.

We used Review Manager 5.3 software for statistical analysis. To evaluate the association between MG patients and the SARS-CoV-2 vaccines, we used single group percentages and corresponding 95% confidence intervals (CIs) and a whole random-effects meta-analysis model to summarize the data. Subgroup analysis was subsequently performed to calculate the percentage of worsening MG and adverse events depending on the vaccine dose. A binary controlled study was used to calculate the worsening MG percentage depending on the gender, antibody positive, and type of MG. In the random-effects meta-analysis model, the odds ratio (OR) and 95% CI were used to evaluate the effect. The I^2 and P values were used to quantify the heterogeneity of the effects in the included studies.

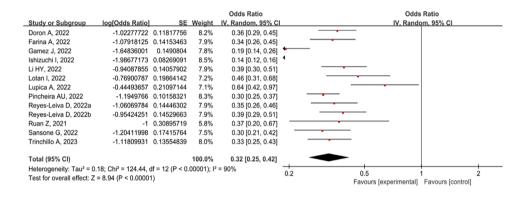
In total, 12 studies involving 1465 patients were included in the final analysis (Table 1) [1–12]. The overall OR for MG worsening after COVID-19 vaccination in MG patients was 0.32 (95% CI, 0.25 to 0.42, P < 0.001) based on 12 studies (Fig. 1). The overall OR for MG worsening after COVID-19 vaccination in males vs. females based on eight studies was 0.59 (95% CI, 0.28 to 1.21, P = 0.15) (Fig. 2A). The overall OR for

 Table 1
 Baseline characteristics

 of the included studies
 Image: Studies

Study	Year	Country	Type of study	Total patients	Male/female
Doron A [2]	2022	Israel	Cross-sectional study	160	89/71
Farina A [3]	2022	Italy	Observational study	104	55/49
Gamez J [4]	2022	Spain	Prospective observational study	91	36/55
Ishizuchi K [5]	2022	Japan	Observational study	343	119/224
Li HY [6]	2022	China	Observational study	107	54/53
Lotan I [7]	2022	Israel	Observational study	55	35/20
Lupica A [8]	2022	Italy	Observational study	90	43/47
Pincheira AU [12]	2022	Canada	Observational study	200	103/97
Reyes-Leiva D [9]	2022	Spain	Prospective observational study	100	45/55
Ruan Z [10]	2021	China	A single-center case series	22	16/6
Sansone G [11]	2022	Italy	Retrospective study	80	41/39
Trinchillo, A [1]	2023	Italy	Retrospective study	113	60/53

Fig. 1 Worsening MG after SARS-CoV-2 vaccination in MG patients



MG worsening after COVID-19 vaccination in AchR⁺ vs. MuSK⁺ groups based on six studies was 0.29 (95% CI, 0.10 to 0.69, P < 0.05) (Fig. 2B). The overall OR for MG worsening after COVID-19 vaccination based on eight studies was 0.29 (95% CI, 0.25 to 0.33, P < 0.001) (Fig. 2C). The OR for the first dose of the vaccine was 0.27 (95% CI, 0.20 to 0.38, P < 0.001), the second dose was 0.29 (95% CI, 0.25 to 0.34, P < 0.001), and the third dose was 0.30 (95% CI, 0.25 to 0.35, P < 0.001). These results suggested that a small number of MG patients who received the COVID-19 vaccine had a transient worsening MG. The MG worsening rate in

MG patients with MuSK⁺ was significantly higher than in MG patients with AchR⁺. There was no significant difference in the MG worsening rate after COVID-19 vaccination between genders and different doses of vaccine.

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The results from seven studies showed that the overall OR for adverse events after COVID-19 vaccination in MG patients was 0.67 (95% CI, 0.56 to 0.79, P < 0.001). The OR of the first dose vaccine was 0.65 (95% CI, 0.47 to 0.91, P = 0.01), the second dose vaccine was 0.71 (95% CI, 0.56 to 0.91, P = 0.007), and the third dose vaccine was 0.58 (95% CI, 0.47 to 0.72, P < 0.001) (Fig. 3). The

Fig. 2 Worsening MG after SARS-CoV-2 vaccination in MG patients subtyped for gender (**A**), antibody positive (**B**), and dose of vaccine (**C**)

1		202000						19420 (P2.94)		
		Male		Fema			Odds Ratio		Ratio	
							M-H, Random, 95% CI	M-H, Rand	lom, 95% Cl	
	A, 2022	7	89	6	71	20.6%	0.92 [0.30, 2.89]			
	A, 2022	1	55	7	49	9.0%	0.11 [0.01, 0.94]			
	hi I, 2022	0	119	3	224	5.2%	0.26 [0.01, 5.17]	100 C		
Li HY, :		6	54	5	53	18.6%	1.20 [0.34, 4.20]			
Lotan I		7	35	1	20	8.8%	4.75 [0.54, 41.80]			
	A, 2022	4	29	10	24	17.3%	0.22 [0.06, 0.85]			
Ruan Z		1	16	1	6	5.3%	0.33 [0.02, 6.37]			
Trinchi	llo A, 2023	3	60	5	53	15.2%	0.51 [0.11, 2.22]			
Total (95% CI)		457		500	100.0%	0.59 [0.28, 1.21]	-	+	
Total e	vents	29		38						
Hetero	geneity: Tau ² = 0	.33; Chi ²	= 10.21	, df = 7	P = 0.1	8); $l^2 = 31$	%			10
Test fo	r overall effect: Z	= 1.45 (F	P = 0.15)				0.01 0.1 Favours [experimental]	1 10 Favours [control]	10
		AChi		MuS			Odds Ratio		Ratio	
Study	or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Rand	lom, 95% Cl	
Doror	n A, 2022	10	129	C			0.44 [0.02, 9.76]	100 million (100 million)		
Farina	a A, 2022	4	83	3	9	31.4%	0.10 [0.02, 0.56]			
Ishizu	ichi I, 2022	2	239	1	15	15.7%	0.12 [0.01, 1.38]		-	
Li HY	, 2022	7	67	C	4	10.5%	1.12 [0.05, 22.83]	25	-	
Lupica	a A, 2022	9	35	1	5	17.6%	1.38 [0.14, 14.07]		•	
Trinch	hillo A, 2023	6	89	1	3	14.8%	0.14 [0.01, 1.83]		<u> </u>	
Total	(95% CI)		642		38	100.0%	0.26 [0.10, 0.69]	-		
	events	38		6						
	ogeneity: Tau ² =		2 = 5.15	df = 5(P = 0.4	0): $ ^2 = 3\%$		++	l	
	for overall effect:					-,,		0.01 0.1 Favours [experimental]	1 10	10
	y or Subgroup	log[Oc	dds Rat	io]	SE	E Weight	Odds Ratio IV. Random. 95% Cl		Ratio	
1.4.1	First dose						IV. Random. 95% CI		Ratio	
1.4.1 Doror	First dose n A, 2022	-1.	869231	72 0.1	158595	5 7.8%	IV. Random. 95% CI 0.15 [0.12, 0.19]		Ratio	
1.4.1 Doror Farina	First dose n A, 2022 a A, 2022	-1. -1.	869231 527200	72 0.1 12 0.13	158595	5 7.8% 2 7.2%	IV, Random, 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29]		Ratio	
1.4.1 Doror Farina Li HY	First dose n A, 2022 a A, 2022 7, 2022	-1. -1. -1.	869231 527200 226170	72 0.1 12 0.13 12 0.13	158595 970102 8873278	5 7.8% 2 7.2% 3 7.2%	IV. Random. 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39]		Ratio	
1.4.1 Doror Farina Li HY Lotan	First dose n A, 2022 a A, 2022 7, 2022 n I, 2022	-1. -1. -1. -0.	869231 527200 226170 912044	72 0.1 12 0.13 12 0.13 83 0.19	158595 970102 8873278 9644333	5 7.8% 2 7.2% 3 7.2% 3 5.6%	IV, Random, 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59]		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye	First dose n A, 2022 a A, 2022 7, 2022	-1. -1. -1. -0.	869231 527200 226170 912044 060697	72 0.1 12 0.13 12 0.13	158595 970102 8873278 9644333 9644332	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0%	IV, Random, 95% Cl 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46]		Ratio	
1.4.1 Doror Farina Li HY Lotan Reyes Ruan	First dose n A, 2022 a A, 2022 f, 2022 a I, 2022 s-Leiva D, 2022	-1. -1. -1. -0.	869231 527200 226170 912044 060697	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14	158595 970102 8873278 9644333 9644332	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0%	IV, Random, 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59]		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye Ruan Subto Heter	First dose h A, 2022 a A, 2022 , 2022 s-Leiva D, 2022 z, 2021 otal (95% CI) rogeneity: Tau ² =	-1. -1. -1. -0. -1. 0.13; Chi	869231 527200 226170 912044 060697 ² = 32.1	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5	158595 970102 8873278 9644333 1446302 9895719	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 9 3.4% 38.3%	IV, Random, 95% Cl 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38]		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye Ruan Subto Heter	First dose n A, 2022 a A, 2022 r, 2022 n I, 2022 s-Leiva D, 2022 z, 2021 otal (95% CI)	-1. -1. -1. -0. -1. 0.13; Chi	869231 527200 226170 912044 060697 ² = 32.1	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5	158595 970102 8873278 9644333 1446302 9895719	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 9 3.4% 38.3%	IV, Random, 95% Cl 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38]		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye: Ruan Subte Heter Test f	First dose n A, 2022 a A, 2022 , 2022 s-Leiva D, 2022 z, 2021 otal (95% CI) ogeneity: Tau ² = for overall effect: Second dose	-1. -1. -1. -0. -1. 0.13; Chi	869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001)	158595 3970102 8873276 9644333 1446302 9895719 6 (P < 0.	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 9 3.4% 38.3% 000001); I ²	IV, Random, 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84%		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye: Ruan Subte Heter Test f 1.4.2 Doror	First dose n A, 2022 a A, 2022 y 2022 y 2022 s-Leiva D, 2022 Z, 2021 otal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91	869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0 -1.301	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1	158595 3970102 3873276 9644333 1446302 9895715 6 (P < 0. 180914	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 9 3.4% 38.3% 000001); I ²	IV. Random. 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84%		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye: Ruan Subte Heter Test f 1.4.2 Doror Farina	First dose n A, 2022 a A, 2022 , 2022 , 2022 s-Leiva D, 2022 s-Leiva D, 2022 z, 2021 otal (95% Cl) ogenetily: Tau ² = for overall effect: Second dose n A, 2022 a A, 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0 -1.301 500602	72 0.1 12 0.13 12 0.13 13 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14	1158595 3970102 3873278 9644333 1446302 9895715 6 (P < 0. 180914 1398054	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 3 3.4% 38.3% 00001); I ² 4 7.8%	IV. Random. 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30]		Ratio	
1.4.1 Doror Farina Li HY Lotan Ruan Subto Heter Test f 1.4.2 Doror Farina Li HY	First dose n A, 2022 a A, 2022 y 2022 y 2022 y 2022 y 2022 Z, 2021 total (95% CI) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 a A, 2022 y 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1.	869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0 -1.301 500602 180890	72 0.1 12 0.13 12 0.13 83 0.18 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14	1158595 3970102 3873278 9644333 1446302 9895715 6 (P < 0. 1180914 1398054 1593933	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 3 38.3% 000001); l ² 4 7.8% 4 7.0% 3 7.0%	IV, Random, 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41]		Ratio	
1.4.1 Doror Farina Li HY Lotan Ruan Subto Heter Test f 1.4.2 Doror Farina Li HY Lotan	First dose h A, 2022 a A, 2022 y 2022 y 2022 y 2022 z, 2021 otal (95% CI) ogeneity: Tau ² = for overall effect: Second dose h A, 2022 y 2022 y 2022 y 2022 y 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1.	869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0 -1.301 500602 180890 070037	72 0.1 12 0.13 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20	158595 3970102 3873276 3873276 38953276 3895715 446302 3895715 467433 395715 4746302 4746302	5 7.8% 2 7.2% 3 5.6% 2 7.0% 3 3.4% 38.3% 00001); l ² 4 7.8% 4 7.8% 5.5%	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.34 [0.23, 0.51]		Ratio	
1.4.1 Doror Farin: Li HY Lotan Reye: Ruan Subte Heter Test f 1.4.2 Doror Farin: Li HY Lotan Reye:	First dose 1 A, 2022 a A, 2022 1, 2022 2, 2022 2, 2022 2, 2021 0 colal (95% Cl) cogeneity: Tau ² = for overall effect: Second dose 1 A, 2022 a A, 2022 1, 2022 1, 2022 2, 2022 1, 2022 2, 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -0.	869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0 -1.301 500602 180890 070037 954242	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20 51 0.14	158595 3970102 3873276 3644333 446302 3895715 4(P < 0. 180914 1398054 1593933 3219901 529663	5 7.8% 2 7.2% 3 5.6% 2 7.0% 3 3.4% 38.3% 00001); l ² 4 7.8% 4 7.0% 3 7.0% 3 7.0% 3 7.0%	IV. Random. 95% Cl 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.27, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.34 [0.23, 0.51] 0.38 [0.29, 0.51]		Ratio	
1.4.1 Doror Farina Li HY Lotan Ruan Subte Heter Test f 1.4.2 Doror Farina Li HY Lotan Reye: Sanse	First dose h A, 2022 a A, 2022 y 2022 y 2022 y 2022 y 2022 y 2022 y 2021 otal (95% CI) ogeneity: Tau ² = for overall effect: Second dose h A, 2022 a A, 2022 y 2022 s-Leiva D, 2022 s-Leiva D, 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -0.	869231 527200 226170 912044 060697 ² = 32.1 (P < 0.0 -1.301 500602 180890 070037 954242	72 0.1 12 0.13 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20	158595 3970102 3873276 3644333 446302 3895715 4(P < 0. 180914 1398054 1593933 3219901 529663	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 3 38.3% 000001); l ² 4 7.8% 4 7.0% 3 7.0% 1 5.5% 3 7.0% 2 6.6%	IV, Random, 95% Cl 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.34 [0.23, 0.51] 0.39 [0.29, 0.51] 0.28 [0.20, 0.38]		Ratio	
1.4.1 Doror Farina Li HY Lotan Reye: Ruan Subtt Heter Test f 1.4.2 Doror Farina Li HY Lotan Reye: Sanst Subtt Heter	First dose 1 A, 2022 a A, 2022 1, 2022 2, 2022 2, 2022 2, 2021 0 colal (95% Cl) cogeneity: Tau ² = for overall effect: Second dose 1 A, 2022 a A, 2022 1, 2022 1, 2022 2, 2022 1, 2022 2, 2022	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -1. -0. -1 0.01; Chi	869231 527200 226170 912044 060697 2 = 32.1 (P < 0.0 -1.301 500602 180890 070037 954242 1.27875 2 = 8.33	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20 51 0.14 36 0.16 , df = 5	158595 8970102 8873276 6644333 1446302 0895715 6 (P < 0. 1180914 1398054 1593933 0219901 1529663 3018082	5 7.8% 2 7.2% 3 5.6% 2 7.0% 3 5.6% 2 7.0% 3 3.4% 38.3% 37.3% 38.3% 37.3%	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.27, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.37 [0.20, 0.63] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.38 [0.29, 0.51] 0.38 [0.29, 0.51] 0.28 [0.20, 0.38]		Ratio	
1.4.1 Doror Farina Li HY Lotan Ruan Subto Heter Test f 1.4.2 Doror Farina Li HY Lotan Reye: Sanso Subto Heter Test f	First dose n A, 2022 a A, 2022 i, 2022 i, 2022 z, 2022 z, 2021 otal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 i, 2022 s-Leiva D, 2022 s-Leiva D, 2022 one G, 2022 otal (95% Cl) ogeneity: Tau ² = for overall effect:	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -1. -0. -1 0.01; Chi	869231 527200 226170 912044 060697 2 = 32.1 (P < 0.0 -1.301 500602 180890 070037 954242 1.27875 2 = 8.33	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20 51 0.14 36 0.16 , df = 5	158595 8970102 8873276 6644333 1446302 0895715 6 (P < 0. 1180914 1398054 1593933 0219901 1529663 3018082	5 7.8% 2 7.2% 3 5.6% 2 7.0% 3 5.6% 2 7.0% 3 3.4% 38.3% 37.3% 38.3% 37.3%	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.27, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.37 [0.20, 0.63] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.38 [0.29, 0.51] 0.38 [0.29, 0.51] 0.28 [0.20, 0.38]		Ratio	
1.4.1 Doror Farina: Li HY Lotan Ruan Subte Heter Test f 1.4.2 Doror Farina: Li HY Lotan Reye: Subte Heter Test f 1.4.3	First dose n A, 2022 a A, 2022 , 2022 I, 2022 Z, 2022 Z, 2021 otal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 a A, 2022 I, 2022 I, 2022 J, 202 J, 2022 J, 202 J, 2022 J, 202 J, 202 J, 202 J, 202 J,	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -0. -1. 0.01; Chi Z = 15.60	869231 527200 912044 060697 2 = 32.1 (P < 0.0 -1.301 500602 180890 070037 954242 1.27875 2 = 8.33 0 (P < 0.0	72 0.1 12 0.13 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20 51 0.14 36 0.16 , df = 5 00001)	158596 15873278 1644333 1446302 1895719 180914 1398054 1593933 1219901 1529663 1529	5 7.8% 3 7.2% 3 5.6% 2 7.0% 3 38.3% 00001); l ² 4 7.8% 4 7.0% 3 7.0% 4 7.8% 4 7.0% 3 7.0% 4 0.6% 4 0.8% 40.8%	IV. Random. 95% CI 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.38 [0.29, 0.51] 0.28 [0.20, 0.38] 0.29 [0.25, 0.34] %		Ratio	
1.4.1 Doror Farina Li HY Lotan Ruan Subte Heter Test f 1.4.2 Doror Farina Li HY Lotan Reyee Sanse Subte Heter Test f	First dose n A, 2022 a A, 2022 ; 2022 i, 2022 i, 2022 z, 2021 otal (95% CI) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 a A, 2022 s-Leiva D, 2022 s-Leiva D, 2022 otal (95% CI) ogeneity: Tau ² = for overall effect: Third dose n A, 2022	-1. -1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -0. -1 0.01; Chi Z = 15.60	869231 527200 912044 060697 2 = 32.1 (P < 0.0 -1.301 500602 180890 070037 954242 1.27875 2 = 8.33 0 (P < 0.0	72 0.1 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20 51 0.14 36 0.16 , df = 5 00001) 47 0.12	158596 15873278 1644333 1446302 1895719 180914 1398054 1593933 1219901 1529663 1529	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 3 3.4% 38.3% 00001); l ² 4 7.8% 4 7.8% 4 7.8% 4 7.0% 3 7.0% 2 6.6% 40.8% 40.8% 4); l ² = 40'	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.38 [0.29, 0.41] 0.39 [0.29, 0.51] 0.39 [0.29, 0.51] 0.39 [0.20, 0.34] 0.29 [0.25, 0.34] %		Ratio	
1.4.1 Doror Farina: Li HY Lotan Reyee Ruan Subte Heter Test f 1.4.2 Doror Farina: Li HY Lotan Reyee Sanse Subte Heter Test f 1.4.3 Doror Farina: Trinct	First dose n A, 2022 a A, 2022 ; 2022 ; 2022 ; 2022 Z, 2021 odal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 ; 2022 ; 2022 ; 2022 i, 2022 one G,	-1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -1. -1. -1. -1. -1. -1. -1.	869231 527200 226170 912044 060697 2 = 32.1 500602 -1.301 500602 180890 954242 .27875 2 = 8.33 ((P < 0. 325652 168792	72 0.1 12 0.13 83 0.19 84 0.14 -1 0.30 6, df = 5 0001) 03 0.1 35 0.14 14 0.14 87 0.20 51 0.14 36 0.16 , df = 5 00001) 47 0.12	1158599 1970102 1970102 1970102 1970102 1970102 1970102 1980571 19805771 19805777 19805777 19805777 19805777 19805777 198057777 19805777 19805777 19805777 19805777 19805777 19805777 19805777 19805777 19805777 19805777 19805777 19805777	5 7.8% 2 7.2% 3 7.2% 3 7.2% 3 5.6% 2 7.0% 3 8.3% 000001); 1 ² 4 7.8% 4 7.8% 4 7.0% 3 7.0% 1 5.5% 3 7.0% 2 6.6% 40.8% 40; 1 ² = 40' 3 7.6% 9 6.0% 9 7.3%	IV. Random. 95% Cl 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.22, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.38 [0.29, 0.51] 0.28 [0.20, 0.38] 0.29 [0.25, 0.34] %		Ratio	
1.4.1 Doror Farina: Li HY Lotan Reyee: Ruan Subtx Heter Test f 1.4.2 Doror Farina: Li HY Lotan Reyee: Sans: Subtx Heter Test f 1.4.3 Doror Farina: Doror Farina: Subtx Heter Test f 1.4.3 Doror	First dose n A, 2022 a A, 2022 i, 2022 i, 2022 z, 2022 z, 2021 otal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 a A, 2022 i, 2022 s-Leiva D, 2022 one G, 2022	$\begin{array}{c} -1.\\ -1.\\ -1.\\ -2.\\ -1.\\ 0.13; Chi Z = 7.91 (-1.) \\ -1.\\ -1.\\ -2.\\ -1.\\ -0.\\ -1\\ 0.01; Chi Z = 15.60\\ -1.\\ -1.\\ -1.\\ 0.00; Chi \end{array}$	8692311 527200 226170 912044 060697 -1.301 500602 180890 7/037 2 = 8.33 ((P < 0. 325652 168792 118099 2 = 1.37	72 0.1 12 0.1 13 0.1 14 0.1 15 0 0.1 10 0	1158599 1970102 1873277 1873277 1844330 1846300 18895715 19707 188914 199071 199071 199071 199071 1990777 1990777 1990777 1990777 1990777 1990777 1990777	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 3 3.4% 3 8.3% 00001); l ² 4 7.8% 4 7.0% 3 7.0% 4 0.8% 4 0.8% 4 4); l ² = 40' 3 7.6% 9 6.0% 9 7.3% 2 0.9%	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.77, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.41] 0.39 [0.29, 0.51] 0.39 [0.29, 0.51] 0.28 [0.20, 0.38] 0.29 [0.25, 0.34] %		Ratio	
1.4.1 Doror Farina: Li HY Lotan Subte Heter Test f 1.4.2 Doror Farina: Li HY Lotan Reye: Subte Heter Test f 1.4.3 Doror Farina: Trinch Subte Heter Test f	First dose n A, 2022 a A, 2022 ; 2022 ; 2022 ; 2022 Z, 2021 otal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 ; 2022 s-Leiva D, 2022 one G, 2022 a A, 2022 a A, 2022 a A, 2022 a A, 2022 a A, 2022 a A, 2023 a A, 2024 a A, 2025 a	$\begin{array}{c} -1.\\ -1.\\ -1.\\ -2.\\ -1.\\ 0.13; Chi Z = 7.91 (-1.) \\ -1.\\ -1.\\ -2.\\ -1.\\ -0.\\ -1\\ 0.01; Chi Z = 15.60\\ -1.\\ -1.\\ -1.\\ 0.00; Chi \end{array}$	8692311 527200 226170 912044 060697 -1.301 500602 180890 7/037 2 = 8.33 ((P < 0. 325652 168792 118099 2 = 1.37	72 0.1 12 0.1 13 0.1 14 0.1 15 0 0.1 10 0	1158599 1970102 1873277 1873277 1844330 1846300 18895715 19707 188914 199071 199071 199071 199071 1990777 1990777 1990777 1990777 1990777 1990777 1990777	5 7.8% 2 7.2% 3 7.2% 3 5.6% 2 7.0% 3 3.4% 3 3.3% 00001); l ² 4 7.8% 4 7.0% 3 7.0% 3 7.0% 2 6.6% 40.8% 40.8% 40.8% 9 6.0% 9 7.3% 2 0.9% 1 ² = 0%	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.17, 0.29] 0.29 [0.22, 0.39] 0.40 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.37 [0.20, 0.63] = 84% 0.27 [0.22, 0.34] 0.28 [0.20, 0.41] 0.39 [0.29, 0.51] 0.39 [0.29, 0.51] 0.29 [0.25, 0.34] %		Ratio	
1.4.1 Doror Farina: Li HY Lotan Reyee: Ruan Subte Heter Test f 1.4.2 Doror Farina: Li HY Lotan Reyee: Sanse Subte Heter Test f 1.4.3 Doror Farina: Trinck Subte Heter Test f 1.4.3 Doror Farina: Trinck Subte Heter Total	First dose n A, 2022 a A, 2022 i, 2022 i, 2022 z, 2022 z, 2021 otal (95% Cl) ogeneity: Tau ² = for overall effect: Second dose n A, 2022 i, 2022 i, 2022 s-leiva D, 2022 one G, 2022 otal (95% Cl) ogeneity: Tau ² = for overall effect: Third dose n A, 2023 i A, 2022 a A, 2022 i A, 2022 i A, 2023 i A, 2023 i A, 2023 i A, 2023 i A, 2023 otal (95% Cl) ogeneity: Tau ² =	-1. -1. -1. -1. -0. -1. 0.13; Chi Z = 7.91 (-1. -1. -1. -1. -1. -1. -1. -1.	8692311 527200 226170 912044 060697 ² = 32.1 P < 0.0 -1.301 500602 070037 954242 .27875 ² = 8.33 10 (P < 0. 325652 118099 ² = 1.37 (P < 0.	72 0.12 0.12 12 0.12 13 0.12 13 0.12 14 0.12 14 0.14 14 0.14 15 0.20 15 0.14 14 0.14 15 0.20 15 0.14 15 0.14	1158599 1970102 187327{ 1644332 180914 180914 180914 19905715 19907 152966 1018082 121990 152966 121990 152963 121990 152965 121990 121990 121990 121990 121990 121990 121990 121990 121990 121990 121990 121900 121990 121990 121990 1219000 1219000 1219000 1219000 1219000 1219000 1219000 1	5 7.8% 2 7.2% 3 7.2% 3 7.2% 3 7.2% 3 7.2% 3 7.2% 3 7.2% 3 7.0% 4 7.8% 4 7.8% 4 7.8% 4 7.8% 4 7.8% 4 7.8% 3 7.0% 3 7.0% 4 7.8% 4 7.0% 3 7.0% 3 7.0% 4 7.8% 4 7.0% 3 7.0% 4 7.8% 4 7.0% 3 7.0% 4 7.8% 4 7.0% 3 7.0% 4 7.0% 3 7.0% 4 7.8% 4 7.0% 3 7.0% 4 7.0% 4 7.8% 4 7.0% 3 7.0% 4 7.8% 4 7.0% 4 7.0% 3 7.0% 4 7.8% 4 7.0% 4 7.8% 4 7.0% 4 0.0% 4 7.0% 4 0.0% 4 0.0%	IV. Random. 95% Cl. 0.15 [0.12, 0.19] 0.22 [0.27, 0.29] 0.29 [0.27, 0.59] 0.35 [0.26, 0.46] 0.37 [0.20, 0.67] 0.27 [0.20, 0.38] = 84% 0.27 [0.22, 0.34] 0.22 [0.17, 0.30] 0.31 [0.23, 0.51] 0.38 [0.29, 0.51] 0.28 [0.20, 0.38] 0.29 [0.25, 0.34] %		Ratio	

subgroup analysis did not show any significant differences within subgroups based on the dose of vaccine.

In conclusion, the results of our meta-analysis showed that few MG patients who received the SARS-CoV-2 vaccines experienced a transient worsening MG. The worsening MG rate in MG patients with MuSK⁺ was significantly higher than in MG patients with AchR⁺. Anti-MuSK-ab positivity is an independent risk factor for disease deterioration and is associated with poor outcome of myasthenic crisis [13]. In addition, the MuSK-MG subtype Fig. 3 Adverse events after SARS-CoV-2 vaccination in MG patients subtyped for dose of vaccine

			Odds Ratio	Odds Ratio				
Study or Subgroup	log[Odds Ratio]	E Weight	IV, Random, 95% CI	IV. Random, 95% CI				
1.5.1 First dose								
Doron A, 2022	-0.86530143 0.1193410		0.42 [0.33, 0.53]					
Farina A, 2022	-0.65066532 0.1462193	6.6%	0.52 [0.39, 0.69]					
Gamez J, 2022	0.00954532 0.1822394	6.0%	1.01 [0.71, 1.44]					
Lotan I, 2022	-0.50930594 0.204917	39 5.6%	0.60 [0.40, 0.90]					
Lupica A, 2022	-0.32585358 0.215976	16 5.4%	0.72 [0.47, 1.10]					
Pincheira AU, 2022	0.17609126 0.132287	6.8%	1.19 [0.92, 1.55]	+				
Reyes-Leiva D, 2022	-0.78837042 0.147064		0.45 [0.34, 0.61]					
Subtotal (95% CI)		43.9%	0.65 [0.47, 0.91]					
Heterogeneity: Tau ² = 0	.17; Chi ² = 48.42, df = 6 (P <	0.00001); l ² :	= 88%					
Test for overall effect: Z	= 2.53 (P = 0.01)							
1.5.2 Second dose								
Doron A, 2022	-0.62838893 0.123312	6.9%	0.53 [0.42, 0.68]	_ _				
Farina A, 2022	-0.61887349 0.151202		0.53 [0.42, 0.88]	_ _				
Gamez J, 2022	-0.08813609 0.177887		0.92 [0.65, 1.30]					
Lotan I, 2022	-0.38021124 0.2176823		0.68 [0.45, 1.05]					
Lupica A, 2022	-0.14893901 0.226110		0.86 [0.55, 1.34]					
Pincheira AU, 2022	0.10473535 0.1279204		1.11 [0.86, 1.43]					
Reyes-Leiva D, 2022	-0.5754078 0.150520		0.56 [0.42, 0.76]					
Subtotal (95% CI)		43.5%	0.71 [0.56, 0.91]	\bullet				
Heterogeneity: Tau ² = 0.08; Chi ² = 26.11, df = 6 (P = 0.0002); l ² = 77%								
Test for overall effect: Z	= 2.69 (P = 0.007)							
1.5.3 Third dose								
Doron A, 2022	-0.51723848 0.13161	6.8%	0.60 [0.46, 0.77]					
Farina A, 2022	-0.58502665 0.189401	73 5.9%	0.56 [0.38, 0.81]					
Subtotal (95% CI)		12.7%	0.58 [0.47, 0.72]	•				
Heterogeneity: Tau ² = 0.00; Chi ² = 0.09, df = 1 (P = 0.77); l ² = 0%								
Test for overall effect: Z = 4.99 (P < 0.00001)								
Total (95% CI)		100.0%	0.67 [0.56, 0.79]	◆				
Heterogeneity: Tau ² = 0	.10; Chi ² = 77.65, df = 15 (P <	0.00001); 12	² = 81%					
Test for overall effect: Z		,, -		0.2 0.5 1 2 5				
Test for subaroup different	ences: Chi ² = 1.46. df = 2 (P =	0.48). I ² = 0	%	Favours [experimental] Favours [control]				

is deficient in both central and peripheral B-cell tolerance checkpoints, where the major role appears to be played by plasmablasts [14]. The COVID-19 vaccine could stimulate circulating autoreactive B cells and make MuSK-MG patients more susceptible. The SARS-CoV-2 vaccines are relatively safe for MG patients. Therefore, we encouraged patients with well-controlled MG vaccinated SARS-CoV-2 vaccine, unless there was a specific contraindication.

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Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval and Informed consent None.

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