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COVID-19

Safety of COVID-19 vaccine in patients with epilepsy: a meta-analysis

Qian Zheng[1] · Pengfei Ma[1] · Zhanhui Feng[1]

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Letter to the Editor:

Coronavirus Disease 19 (COVID-19), caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has been associated with greater than two million deaths worldwide. The safety of the COVID-19 vaccine for patients with epilepsy has been examined. Many observational trials of COVID-19 vaccine in patients with epilepsy have been analyzed using a systematic search of common databases between January 1, 2020, and August 20, 2022.

We read with great interest the study in this journal by Romozzi et al., who found that only a small percentage of vaccinated people with epilepsy had a transient short-term increase of seizure frequency [1]. However, new-onset refractory status epilepticus following the ChAdOx1 nCoV-19 vaccine was reported by one study [2]. Hence, meta-analysis of the safety of COVID-19 vaccine in patients with epilepsy is of great importance. An extensive literature search was performed in PubMed, Web of Science, EMBASE, and Cochrane Library to find all relevant studies published from January 1, 2020, to August 20, 2022. We screened the references of the retrieved studies and restricted the language of the search to English. The following keywords were used in the search: COVID-19 vaccines (SARS-CoV-2 vaccines, SARS2 vaccines, SARS coronavirus 2 vaccines, coronavirus disease 2019 vaccines, 2019-nCoV vaccine, and 2019 novel coronavirus vaccines) and epilepsy (epilepsies, seizure). The inclusion criteria included (1) patients diagnosed with epilepsy who received COVID-19 vaccines, and (2) use of English. The exclusion criteria were as follows: (1) irrelevant to the research direction, (2) no relevant data, (3) case reports, (4) repeated articles, and (5) review papers.

The analysis was conducted using Review Manager statistical software, version 5.3. Single group percentages and corresponding 95% confidence intervals (CIs) were used to assess the association between patients with epilepsy and the COVID-19 vaccine in a whole random-effects meta-analysis model. Subgroup analysis was conducted for calculating the adverse events percentage depending on the type and dose of vaccine. The I^2 and P values were used to quantify the heterogeneity of the effects among the included studies.

A total of seven observational studies involving 958 patients were identified in the final analysis, and the details of the included studies are listed in Table 1 [1, 3–8]. Six studies showed that the overall odds ratio (OR) for worsening seizure following COVID-19 vaccination in epilepsy patients subtyped for type of vaccine was 0.30 (95% CI 0.22 − 0.41, $P < 0.001$), the mRNA-based vaccine was 0.29 (95% CI 0.21 − 0.41, $P < 0.001$), and the vector-based vaccine was 0.33 (95% CI 0.14 − 0.75, $P = 0.008$) (Fig. 1A). There was no significant difference in worsening seizures following COVID-19 vaccination between the mRNA-based vaccine and vector-based vaccine ($P = 0.80$). Five studies showed that the overall OR of worsening seizures following COVID-19 vaccination in epilepsy patients subtyped for dose of vaccine was

Qian Zheng and Pengfei Ma are the co-first authors.

✉ Zhanhui Feng
h9450203@126.com

[1] Department of Neurology, Affiliated Hospital of Guizhou Medical University, Guiyang, China

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Table 1 Baseline characteristics of the included studies

Study	Country	Type of study	Total patients	Mean age	Male	Vaccine type (number of patients)
Chan CC	China	Cross-sectional study	200	45	101	BioNTech vaccine ($n=71$) Sinovac vaccine ($n=35$)
Yang XY	China	Cross-sectional study	77	14.91	35	BBIBP-CorV ($n=58$) Ad5-nCoV ($n=16$) ZF2001($n=2$) Inactivated (Vero Cells) ($n=1$)
Romozzi M	Italy	Multicentric observational cohort study	358	47.46	161	Pfizer/BNT162b2 ($n=257$) Moderna/mRNA1273 ($n=43$) AstraZeneca/AZD122/ChAdOx1 n-CoV-19 ($n=24$) Janssen/Ad26 ($n=1$)
Wrede RV	Germany	Observational study	54	47.9	27	BioNTech mRNA ($n=26$) Moderna mRNA ($n=8$) Astra Zeneca vector ($n=18$)
Clayton LM	UK	Cross-sectional study	9	unknown	unknown	Pfifizer/BioNTech ($n=2$) Oxford/AstraZeneca ($n=7$)
Massoud F	Kuwait	Cross-sectional study	82	33.204	33	BNT162b2 mRNA ($n=50$) ChAdOx1 nCoV-19 ($n=32$)
Özdemir HN	Turkey	Cross-sectional study	178	29	87	BNT162b2 mRNA ($n=136$) CoronaVac ($n=35$) Combination ($n=7$)

0.25 (95% CI 0.16 – 0.41, $P<0.001$), the single dose vaccine was 0.25 (95% CI 0.14 – 0.44, $P<0.001$), and the double dose vaccine was 0.27 (95% CI 0.11 – 0.66, $P=0.004$) (Fig. 1B). There was no significant difference in worsening seizures following COVID-19 vaccination between single and double doses of the vaccine ($P=0.89$).

In four studies, we found that the overall OR of local adverse events in epilepsy patients following COVID-19 vaccination was 0.82 (95% CI 0.65 – 1.05, $P=0.11$), the mRNA-based vaccine was 0.86 (95% CI 0.57 – 1.29, $P=0.46$), and the vector-based vaccine was 0.92 (95% CI, 0.50 – 1.69, $P=0.78$) (Fig. 2A). In two studies, we found that overall OR systemic adverse events in epilepsy patients following COVID-19 vaccination was 0.73 (95% CI, 0.53 – 1.00, $P=0.05$), the mRNA-based vaccine was 0.65 (95% CI 0.51 – 0.83, $P<0.001$), and the vector-based vaccine was 1.12 (95% CI, 0.55 – 2.24, $P=0.76$) (Fig. 2B). There was no significant difference in local and systemic adverse events in epilepsy patients following COVID-19 vaccination between the mRNA-based vaccine and vector-based vaccine.

In conclusion, our research showed that a small percentage of vaccinated patients with epilepsy had a transient short-term increase of seizure frequency. The current COVID-19 vaccine for patients with epilepsy was safe. We found that the mRNA vaccine was relatively safer than the vector-based vaccine for patients with epilepsy. Future studies should determine adverse events of each vaccine type and critically identify mechanisms of severe adverse events following vaccination.

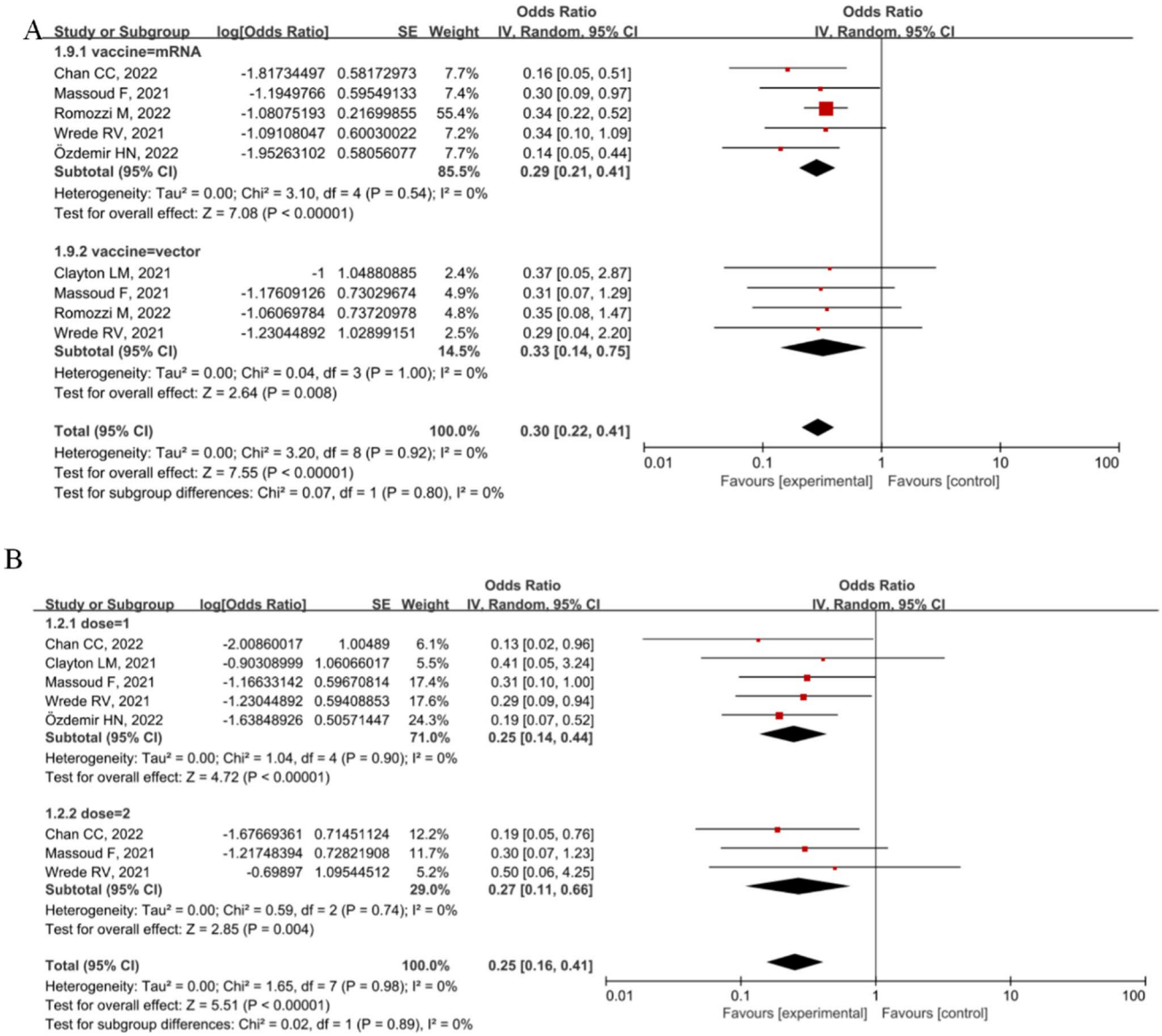

Fig. 1 Worsening seizures following COVID-19 vaccination in patients with epilepsy subtyped for type of vaccine (**A**) and dose of vaccine (**B**)

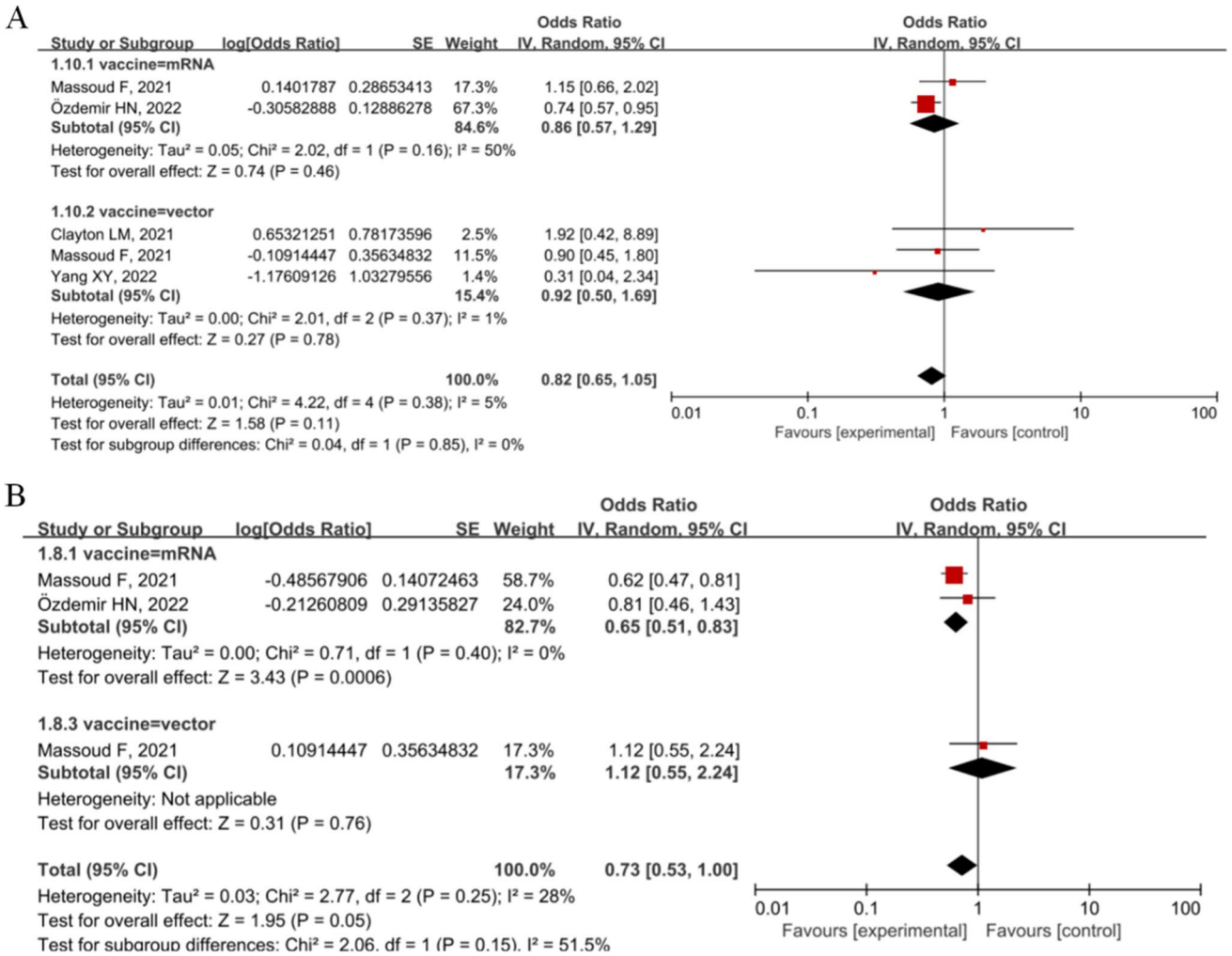

Fig. 2 Local adverse events (**A**) and systemic adverse events (**B**) following COVID-19 vaccination in patients with epilepsy subtyped for type of vaccine

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Declarations

Ethical approval None.

Conflicts of interest The authors declare that they have no conflicts of interest.

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