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# © Clinical characterization and treatment outcomes of intracerebral and subarachnoid hemorrhage after vaccination against COVID-19: A systematic review of the literature

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#### **ICH COVID Vaccine**



As the number of COVID-19 vaccines increases, reports of complications are also increasing. In particular, when cerebral hemorrhage occurs, the prognosis is poor. Here, we aimed to investigating the clinical course of patients who developed intracerebral hemorrhage after COVID-19 vaccination and the patient prognosis through a systematic review.

As coronavirus disease 2019 (COVID-19) hit the world like never before, there were 244,105,621 infection cases and 4,959,347 deaths worldwide as of October 24, 2021. As the number of vaccination increases, reports of death and serious adverse reactions after vaccination are also increasing.

DOI

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#### 1 Review title

Clinical characterization and treatment outcomes of intracerebral and subarachnoid hemorrhage after vaccination against COVID-19: A systematic review of the literature

# 2 Anticipated or actual start date

20 Novermber 2021

# 3 Anticipated completion date

20 February 2022

# 4 Stage of review at time of this submission

Review stage	Started	Completed
Review starge	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

#### 5 Funding sources/sponsors

This study received funding from the National Research Foundation of Korea funded by the Ministry of Education

Grant number(s) 2020R1I1A3070726 2021R1A6A3A01087921

#### **Conflict of interest**



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None

#### 7 Review question

Participants: Patients of intracerebral and subarachnoid hemorrhage after vaccination against COVID-19

Exposure: Vaccination against COVID-19

Type of vaccination: To compare complications based on various vaccine types

Outcome: Presence of ICH, cerebral venous thrombosis (CVT), thrombosis with thrombocytopenia syndrome (TTS), death

#### 8 Searches

MEDLINE, EMBASE, and Google Scholar

# 9 Condition or domain being studied

As the number of COVID-19 vaccines increases, reports of complications are also increasing. In particular, when cerebral hemorrhage occurs, the prognosis is poor. Here, we aimed to investigating the clinical course of patients who developed intracerebral hemorrhage after COVID-19 vaccination and the patient prognosis through a systematic review.

As coronavirus disease 2019 (COVID-19) hit the world like never before, there were 244,105,621 infection cases and 4, 959,347 deaths worldwide as of October 24, 2021. As the number of vaccination increases, reports of death and serious adverse reactions after vaccination are also increasing.

#### 10 Participants/population

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion criteria (Pai 2021):

- 1. A patient who visited the hospital for ICH after receiving COVID-19 vaccine
- 2. ICH that occurred within 28 days after vaccination
- 3. Spontaneous cerebral hemorrhage

Exclusion criteria:

- 1. ICH after COVID-19 infection
- 2. Patients with ICH without prior history of COVID-19 vaccination
- 3. ICH that are caused by after traumatic brain injury

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4. ICH that occurred beyond 28 days after vaccination

#### **Definitions:**

- 1. COVID-19 vaccine:
- ChAdOx1 nCoV-20' (AZ),
- mRNA (Pfizer and Moderna),
- Ad26.COV2.S (Johnson & Johnson)
- 2. Intracerebral hemorrhage (ICH) was defined as hemorrhage in cerebrum as the predominate lesion. Those with concomitant SAH were included in this study. However, pure SAH alone was not included in this study.
- 3. COVID-19 infection: diagnosed by any means as reported.

#### References:

Pai M, et al. Vaccine-induced prothrombotic immune thrombocytopenia VIPIT following AstraZeneca COVID-19 vaccination: interim guidance for healthcare professionals in emergency department and inpatient setting. Science Brief of the Ontario COVID-19 Science Advisory Table. 2021;1(21).

## 11 Intervention(s), exposure(s)

There is no designated intervention or exposure in this study because the aim of this review is narrative outcome data.

#### 12 Comparator(s)/control

There is no designated intervention or exposure in this study because the aim of this review is narrative outcome data.

#### 13 Types of study to be included

Inclusion criteria: all types of article as long as the data is available

- 1. Randomized studies
- 2. Non-randomized studies
- 3. Studies without control: Case series, case reports, brief communication, or other equivalent

Exclusion criteria:

Study not reported in English

#### 14 Context

Hospital setting

#### 15 Main outcome(s)

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- 1. Presence of intracerebral hemorrhage (ICH)
- 2. Presence of cerebral venous thrombosis (CVT)
- 3. Presence of thrombosis with thrombocytopenia syndrome (TTS)
- 4. Functional outcome measured by modified Rankin scale at discharge

Measures of effect Counts of ICH, CVT, TTS

Timing: within 28 days after receiving COVID-19 vaccine

## 16 Additional outcome(s)

None

## 17 Data extraction (selection and coding)

Dr. Jeon and Dr. Chai work independently on study selection according to the aforementioned inclusion and exclusion criteria. Dr. Jeon and Dr. Chai work independently on extraction of data from included studies using a pre-piloted form.

## 18 Risk of bias (quality) assessment

Outcomes listed below is specified to be assessed using GRADE for quality of evidence and presented in the summary of findings (Guyatt, 2011).

All disagreement and accuracy will be resolved by discussion between Jeon and Chai

#### References:

Gordon H. Guyatt et al. GRADE guidelines: 1. Introduction GRADE evidence profiles and summary of findings tables. Journal of Clinical Epidemiology 64 (2011) 383e394 doi: 10.1016/j.jclinepi.2010.04.026

#### 19 Strategy for data synthesis

**Oualitative:** 

GRADE for the certainty of evidence

Quantitative:

If data is not suitable for pooling, a narrative synthesis will be performed.

## 20 Analysis of subgroups or subsets

None

#### 21 Type and method of review

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Epidemiologic, Meta-analysis, Narrative synthesis, COVID-19, Vaccines

# 22 Language

English

# 23 Other registration details

Will be registered in PROSPERO, with details to be updated when available

# 24 Keywords

COVID vaccine, intracerebral hemorrhage, cerebral venous thrombosis, thrombosis with thrombocytopenia syndrome

# 25 Current review status

Ongoing