Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Thrombosis Research 209 (2022) 84–85

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Letter to the Editors-in-Chief

Safety of COVID-19 vaccination in patients with previous cerebral venous sinus thrombosis

ARTICLE INFO

Keywords
Cerebral venous sinus thrombosis
COVID-19 vaccines

ABSTRACT

Introduction: Cerebral venous sinus thrombosis (CVST) after coronavirus (COVID-19) vaccination has been reported. There are no data about thrombosis risk in prior CVST patients. The objective of the study was to describe short-term serious adverse events to COVID-19 vaccines in patients with history of CVST.

Material and methods: We present an observational prospective study of patients with known CVST who received COVID-19 vaccination. Serious event rates within 30 days after second dose vaccination (except one dose for Janssen) were evaluated, including recurrences, hospital admission and death.

Results: The 62 vaccinated patients received: BNT162b2 (Pfizer-BioNTech) in 43 patients (69.4%), mRNA-1273 (Moderna) in 7 patients (11.3%), AZD1222 (ChAdOx1) in 7 patients (11.3%) and Ad26.COV2.S (Janssen) in 5 patients (8.1%). There were no thrombotic recurrences within 30 days of vaccination (95% confidence interval, 0.0–5.8). There was one death (1.6%), not attributable to the vaccine.

Conclusions: COVID-19 vaccines are safe for previous CVST patients.

1. Introduction

Cerebral venous sinus thrombosis (CVST) is considered one of the rare causes of stroke. CVST mostly affects young women, as the most common risk factors are pregnancy and hormonal contraception, usually associated with other conditions such as obesity or hereditary thrombophilias. Acquired prothrombotic diseases, such as antiphospholipid syndrome or cancer, infections, surgery and trauma are also triggering factors of CVST. Recently, there has been increased attention on the possible enhanced risk for CVST from coronavirus disease (COVID-19) and COVID-19 vaccines [1–3].

CVST patients have an estimated risk of recurrent CVST around 2 events per 100 patient-years and approximately 4 events per 100 patient-years for noncerebral venous thrombosis [4,5], with most events occurring after anticoagulant therapy withdrawal. The rate of recurrence seems to persist with time [6].

In November 2021, the global COVID-19 pandemic had already led to more than 255 million SARS-CoV-2 infections and over 5 million deaths. In parallel, the pandemic situation stimulated the development of effective vaccines and to date more than 7300 million vaccine doses have been administered worldwide [7]. Related adverse events including venous thrombosis have been reported [1–3]. Safety of the COVID-19 vaccines in patients with previous CVST has not been known.

Our aim was to describe short-term serious adverse events to COVID-19 vaccines in patients with history of CVST in a tertiary hospital.

2. Methods

We performed an observational prospective study of all patients diagnosed with CVST at our hospital in the last 25 years. Clinical features, risk factors, treatment received, time until vaccination and type of vaccine were collected. Events occurring within 30 days after second dose vaccination (except one dose for Janssen) were evaluated, mainly recurrence of venous cerebral thrombosis or other locations, hospital admission and mortality.

3. Results

A total of 85 patients were diagnosed with CVST, 10 of them died and 9 patients were lost to follow-up before 2021. Of the remaining 66 patients, 62 (93.9%) were vaccinated and 4 patients (6.1%) refused. The mean age of vaccinated patients was 48.4 years (SD 15.7, range 21–87), 77.4% of them were women. Clinical characteristics are shown in Table 1 (Supplementary data). The transverse sinus was the most common site of thrombosis (65.6%). The main predisposing factors were contraceptive use (50.8%), obesity (38.9%) and hyperhomocysteinemia (34.8%). The different types of vaccines received in our series included BNT162b2 (Pfizer-BioNTech) in 43 patients (69.4%), mRNA-1273 (Moderna) in 7 patients (11.3%), AZD1222 (ChAdOx1) in 7 patients (11.3%) and Ad26.COV2.S (Janssen) in 5 patients (8.1%). Mean time elapsed from CVST to vaccination was 9.9 years (SD 7, range 0.5–26.7). At the time of vaccination, 17 patients (27.9%) were taking anticoagulants. One patient had confirmed SARS-CoV-2 RT-PCR-positive Covid-19 infection prior to vaccination. One patient had symptomatic illness with mild symptoms and confirmed SARS-CoV-2 RT-PCR-positive Covid-19 infection after vaccination with BNT162b2.

There were no recurrences of thrombosis at any location within 30 days of vaccination (95% confidence interval, 0.0–5.8). One patient (1.6%) died 13 days after receiving the second dose of BNT162b2 vaccine. It was a 73-year-old woman with advanced Parkinson's disease and

Abbreviations: CVST, cerebral venous sinus thrombosis; COVID-19, coronavirus; VITT, vaccine-induced immune thrombocytopenia.

https://doi.org/10.1016/j.thromres.2021.12.004
Received 27 October 2021; Received in revised form 1 December 2021; Accepted 3 December 2021
Available online 8 December 2021

deteriorating general condition who was admitted for dehydration and acute renal failure due to refusal of food intake, dying of in-hospital infectious complications, which a priori was not attributable to the vaccine. No other serious adverse events occurred in the follow-up.

4. Discussion

To our knowledge, we present first safety real-world data on COVID-19 vaccines in previous CVST patients, showing no thrombotic recurrences within 30 days. There was only one death, not related to the vaccine.

In multiple countries, unusual and severe thrombotic events have been reported after COVID-19 vaccinations in general population. An increase in the expected rate of CVST and deaths in an apparently healthy population has caused particular concern [3,8]. In rare cases, CVST has been associated with adenovirus-vectored vaccines in the context of vaccine-induced immune thrombocytopenia (VITT) [1,2]. Adenoviruses may interact with platelets, the endothelium and the blood coagulation system causing its activation and, in rare cases, triggering an immunological reaction leading to the development of microthrombi in unusual sites [9]. However, experts conclude that benefits of vaccination outweigh the low risk of postvaccination thrombotic events. In fact, recently retrospective research showed a significantly higher incidence of CVST in two weeks after COVID-19 diagnosis than in people who received an mRNA vaccine against COVID-19 and compared to a matched cohort [10]. Recently, a clinical trial and an analysis of surveillance data for serious vaccine-related adverse outcomes have been published [11,12] showing that COVID-19 vaccines are safe and effective with rare thrombotic events. On the contrary, there are no published data to establish the safety of COVID-19 vaccines in subgroups of patients with a higher likelihood of vein thrombosis, such as those with a history of thrombosis, especially CVST patients.

The main limitation of the study is the sample size which might be insufficient to detect a small increase in thrombotic rate post-vaccination. Moreover, broader multicentric studies would provide a robust database to compare CVST recurrence rates in patients on long term anticoagulation to non anticoagulated at the time of vaccination. Future collaborative studies could address these queries. On the other hand, given the observational nature of the work it was not designed to assess vaccine efficacy.

Our data support that COVID-19 vaccines are safe in previous CVST patients.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.thromres.2021.12.004.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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