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.

Trends in Cardiovascular Medicine 32 (2022) 257–258

Contents lists available at ScienceDirect

Trends in Cardiovascular Medicine

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

Editorial commentary: COVID-19 and COVID-19 vaccination: Observations on thrombosis and thrombocytopenia

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ARTICLE INFO

Keywords:
COVID-19
Thrombosis
Vaccination

When the world was shaken by the coronavirus disease 2019 (COVID-19) pandemic, millions of people lost their lives. As recently reported by the WHO in February 2022, there have been 430,257,564 confirmed cases of COVID-19 globally, including 5,922,047 deaths [1]. It was early on during the pandemic that the world recognised the need for vaccination as a mean of reducing the risk of transmission and the risk of developing serious clinical forms of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Various vaccines of different types using different techniques were soon developed and tested in clinical trials: whole virus, protein subunit, viral vector and nucleic acid (RNA and DNA) [2]. The most commonly used types in the mass vaccination programs worldwide include: those encoding the spike protein antigen of SARS-CoV-2 in mRNA-based technology (BNT162b2 - BioNTech/Pfizer and mRNA1273—Moderna) and adenovirus vector-based vaccines (AstraZeneca, Johnson & Johnson, Gamaleya, CanSino). Inactivated virus vaccines (Sinopharm, Sinovac, Bharat Biotech) are also used in some parts of the world [2].

We learned during the pandemic that the COVID 19 is a highly coagulopathic condition, related to 'thromboinflammation' seen with the inflammation and cytokine storm in severe disease [3] Soon after launching mass vaccination programs worldwide, unique thrombotic events with thrombocytopenia were also noted as a rare complication after vaccination with recombinant adenoviral vector vaccine (ChAdOx1 nCov-19, AstraZeneca) [4]. This unique complication is referred to as vaccine-induced immune thrombotic thrombocytopenia (VITT) or thrombosis with thrombocytopenia syndrome (TTS). Unlike the adenoviral vaccines, vaccination with mRNA vaccines (Comirnaty/BioNTech/Pfizer and mRNA-1273/Moderna) was not associated with cerebral venous sinus thrombosis (CVST) and splanchnic venous thrombosis (SVT) [5].

As described in this paper by Iba et al [6], the pathogenesis of VITT is believed to resemble that of heparin-induced thrombocytopenia (HIT), where platelet-activating anti-platelet factor 4 (anti-PF4) antibodies seem to play a key role. However, antibodies in HIT are bound to aminoacids corresponding to different sites on PF4. Moreover, anti-PF4 in VITT have a stronger binding response to PF4 and PF4-heparin complexes [7].

Whereas anti-PF4 antibodies also have been detected after mRNA vaccination, their optical density tends to be low and they seem to have a poor function in terms of platelet aggregation, as detailed in the paper by Iba et al [6].

In the study by Thiele et al [8], the incidence of anti-PF4/polyanion antibodies in healthy vaccinees (after vaccination with ChAdOx1or BNT162b2) was assessed, together with their ability to induce platelet activation. A total of 19 of 281(6.8%) participants tested positive for anti-PF4/polyanion antibodies postvaccination; ChAdOx1: 8.0%, BNT162b2: 5.6%. Optical densities were mostly low (between 0.5 and 1.0 units; reference range, <0.50), and none of the PF4/polyanion enzyme immunoassay (EIA)- positive samples induced platelet activation in the presence of PF4. Hence, it concluded that pathogenic platelet-activating antibodies that cause VITT do not routinely occur after vaccination [8].

As for the COVID 19 infection itself, the risk ratio of venous thromboembolism at 8–14 days was estimated at 13.86 (95% CI, 12.76 to 15.05), compared to risk ratio of 1.10 (95% CI, 1.02 to 1.18) after ChAdOx1 vaccine and 0.99 (95% CI, 0.90 to 1.08) after BNT162b2 vaccine. While the risk for CVST after ChAdOx1vaccination was higher than that after BNT162b2 vaccination [4.01 (95% CI, 2.08 to 7.71 at 8–14 days) versus 2.57 (95% CI, 0.85 to

DOI of original article: 10.1016/j.tcm.2022.02.008
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https://doi.org/10.1016/j.tcm.2022.03.002

7.78 at 15–21 days)], the risk was still the highest after COVID-19 infection per se (at 13.43 (95% CI, 1.99 to 90.59)) [9].

In summary, the morbidity and mortality associated with SARS-CoV-2 infection remain significantly higher than that seen with vaccination, and importantly, thrombosis is estimated to occur at least 100-fold more often in COVID-19 without vaccination than with vaccination [5].

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