Is COVID-19 vaccination beneficial or harmful to endothelial cells?

Masaki Mogi

COVID-19 vaccination is considered to be effective to overcome the ongoing coronavirus (COVID-19) pandemic. However, the side effects or adverse reactions from vaccination have been highlighted and investigated. Serious side effects from vaccination could cause long-term health problems. As one of the cardiovascular side effects, there has been a focus on myocarditis [1], especially in young men, although cases are rare [2]. However, the vascular effects after COVID-19 vaccination are not well known.

The current report in Hypertension Research by Terentes-Printzios et al. demonstrated that a messenger RNA (mRNA) vaccine, the BNT162b2 vaccine, caused a marked increase in inflammatory markers and deterioration of endothelial function [3]. However, these changes were temporary, with a peak at 1 day after vaccination, and had recovered to baseline at 2 days after vaccination. Thus, they concluded the short-term cardiovascular safety of the vaccine. A very recent study by Jabagi et al. showed that no increase in the incidence of acute myocardial infarction, stroke, or pulmonary embolism was detected 14 days following vaccination with the BNT162b2 vaccine [4]. To date, COVID-19 mRNA vaccination does not seem to have a significant risk of cardiovascular side effects.

According to a previous review paper in Hypertension Research [5], the risk of venous and arterial thromboembolic complications has been reported to be significantly higher in patients with COVID-19 due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-induced indirect endothelial injury, which occurs through the following possible mechanisms: (1) an excessive immune response-induced cytokine storm; (2) local and systemic inflammatory responses such as leukocyte activation; and (3) direct SARS-CoV-2 infection-induced endothelial injury. These could be responsible for endotheliopathy and a hypercoagulable state. SARS-CoV-2 vaccines also trigger innate immunity to promote immunological memory [6]. It cannot be denied that a similar excessive immune response-induced cytokine storm occurs in some subjects after vaccination. However, incidents of thrombosis are not significantly increased with BNT162b2 vaccination compared with SARS-CoV-2 infection, although an elevated risk of myocarditis has been observed in both subjects with BNT162b2 vaccination and those with SARS-CoV-2 infection [7]. Thus, there is no need for concern about BNT162b2 vaccine-induced systemic responses or macro- and microthrombosis.

The direct SARS-CoV-2 infection of endothelial cells should also be considered. Recently, Lei et al. demonstrated that the spike protein reduces angiotensin-converting enzyme 2 (ACE2) expression in endothelial cells, resulting in the impairment of endothelial function. They concluded that vaccination-generated antibodies against the S protein also inhibit S protein-induced endothelial injury and protect against host SARS-CoV-2 infectivity [8]. Thus, COVID-19 vaccination also has the potential to prevent endothelial injury.

Different vaccine types are also considered to have different effects on endothelial function. Vaccination with the ChAdOx1 vaccine tends to rarely show the development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against platelet factor 4 [9]. Moreover, mRNA and adenovirus vector vaccines are varied to induce different immune formation in innate immunity after vaccination [6]. In the present study, Terentes-Printzios et al. showed only the results of BNT162b2 vaccination. Thus, more broad investigations are needed to reach a conclusion on the effects of the vaccines on endothelial function. The possible mechanisms of endothelial dysfunction induced by SARS-CoV-2 infection or the mRNA vaccine BNT162b2 as described above are shown in Fig. 1.

Moreover, vaccination prevents SARS-CoV-2 infection and enables people to go on with their daily lives. There is a fear that increased physical inactivity and sedentary behavior (so-called “staying at home” long-term) during the COVID-19 outbreak will increase the global burden of cardiovascular
disease (CVD) [10]. Such non-communicable diseases induced by communicable diseases should be highlighted as a future perspective in long-term mortality, including that due to CVD, especially in the elderly. Vaccination reduces the need for elderly people to “stay at home” and protects them from lifestyle-related diseases. This effect may be the most powerful tool in CVD prevention by attenuating the impairment of vascular function.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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