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Letter to the Editor

Thrombosis, thrombocytopenia, and cardiovascular complications of mRNA-based anti-SARS-CoV-2 vaccines

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With interest we read the article by Yasmin *et al.* on a systematic review about the cardiovascular complications of mRNAbased anti-SARS-CoV-2 vaccines ^[1]. Included were 17636 patients retrieved from 81 articles ^[1]. It was found that in 17192 cases the Biontech Pfizer vaccine (BPV) was made responsible and in 444 cases the Moderna vaccine (MOV) ^[1]. The most common vaccination related complications were thrombosis followed by ischemic stroke ^[1]. The study is excellent, but has limitations that are cause of concerns and should be discussed thrombotic events due to thrombocytopenia.

Another limitation is that not the entire spectrum of cardiovascular complications and thrombosis were included in the evaluation. A common thrombotic complication not evaluated is venous sinus thrombosis (VST)^[2]. VST should have been included because it is a common complication, most commonly of the Astra Zeneca vaccine (AZV) but has been also described with mRNA-based vaccines. A cardiac complication of SARS-CoV-2 vaccinations not included is Takotsubo syndrome (TTS), also known as broken heart syndrome ^[3]. There is also no mention of arterial hypertension and heart failure as complications of SARS-CoV-2 vaccines. Although only rarely reported ^[4], also endocarditis should be included. Cardiac embolism may not only concern the brain but any of the vascular beds, including the kidneys, guts, and limbs. Therefore, complications such as peripheral artery embolism, mesenteric artery embolism, and renal artery embolism should be included in the review.

Another limitation of the study is that overlaps between the evaluated cardiovascular abnormalities, thrombosis and thrombocytopenia were not assessed. We should know how many of the 254 patients with arrhythmias had pericarditis, myocarditis, or myocardial infarction. We also should know how many patients with cardiovascular complications also had thrombosis or thrombocytopenia. Because thrombocytopenia can be complicated by thrombosis ^[5], we should know in how many of the 13893 patients were thrombotic events due to thrombocytopenia.

What was the pathophysiology of myocardial infarction among the 310 patients included? Atherosclerosis, local thrombosis, embolism, spams, or dissection? Particularly we should know how many of those with thrombosis or thrombocytopenia also had myocardial infarction. Information should be provided about how many of the patients with myocardial infarction had classical cardiovascular risk factors (smoking, hypertension, diabetes, hyperlipidemia).

Another limitation of the study is that cardiac complications of anti-SARS-CoV-2 vaccines often do not develop in isolation but are accompanied by vaccine complications in organs other than the heart. We therefore should know in how many of the patients with cardiac complications, other organs were also affected and to which degree these other manifestations contributed to morbidity and mortality of the vaccines.

We should know how often thrombocytopenia was due to vaccine-induced thrombotic thrombocytopenia (VITT). In how many of the patients with thrombocytopenia (n=1346) were platelet factor-4 (PF-4) antibodies positive?

Overall, the interesting study has limitations that call the results and their interpretation into question. The spectrum of cardiovascular complications to anti-SARS-CoV-2 vaccines is broader than discussed.

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