Short communication

Are the COVID-vaccines cause of cerebral vascular accident (CVA) and others pathologies?

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Introduction

Due to various news about vaccines and the adverse effect they have on society and public health; Fears and inferences have been raised about possible post-COVID vaccine side effects. For this reason, articles were selected that talked about post-vaccine effects, including heart disease, paralysis, thrombosis and neurological effects. In recent times, the population has been inundated with advice from trainers, television news, and especially social media platforms like TikTok, Instagram, Facebook, and WhatsApp groups. Users share opinions and warnings about the dangers of vaccines for public health, particularly regarding COVID-19 vaccines. But, What is an vaccine? How is designed? First we must remember that The merit of Edward Jenner, who recognized as the discoverer of the smallpox vaccine, lies in having demonstrated with practical evidence the protection conferred against the disease by the administration in a healthy child of a material from a person with cowpox lesions. This discovery led to the protection of public health from disease-causing pathogens. A vaccine A vaccine is a substance that acts as a stimulator of the immune system so that it can better protect itself from viruses and other infectious agents. In the 19th century, the French doctor Louis Pasteur developed the second generation of vaccines, among others against cholera or rabies, and introduced the term vaccine in honor of

Jenner's experiments with cows. Table 1 Many influencers claim that COVID vaccines have led to side effects or adverse reactions such as immune disorders, headaches, and heart attacks over the past year. But do we have any reason to believe these claims? Why has public trust in vaccines waned over the last four years since the pandemic began?

Table 1 Phases of vaccine design. During phase 2 and phase 3 trials, volunteers and the scientists conducting the study do not know which volunteers are given the vaccine and who is given the comparator product. This is known as a "double-blind trial," and is necessary to ensure that in their assessments of the safety or effectiveness of the vaccine, neither the volunteers nor the scientists are influenced by who received which product. Once the trial is completed and all the results are obtained, it is revealed to the volunteers and the scientists who conducted the trial who received the vaccine and who received the comparator.

Phase	Action
Phase 1	The vaccine is administered to a small number of volunteers in order to evaluate its safety, confirm that it generates an immune response and determine the correct dose. In this phase, vaccines are typically tested on healthy young adult volunteers.
Phase 2	The vaccine is administered to several hundred volunteers, in order to further evaluate its safety and its ability to generate an immune response. Participants in these trials have the same characteristics (for example, age, sex) as the people to whom the vaccine is planned to be administered. In this phase, multiple trials are usually carried out to evaluate various age groups and different formulations of the vaccine.
Phase 3	The vaccine is administered to thousands of volunteers - and comparisons are made with a similar group of people who were not vaccinated but received a comparator product - in order to determine if the vaccine is effective against the disease and study its safety in a group of much more numerous people. Phase 3 trials are typically conducted in many countries and at numerous locations within each country, to ensure that conclusions about vaccine effectiveness are valid for many different populations.

Source: WHO. (https://www.who.int/es/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/how-are-vaccines-developed).

Since late 2019, we've been in a pandemic era where the world came to a standstill due to SARS-CoV-2 (COVID-19). A race to develop vaccines against the virus ensued. However, doubts persist among the public due to misinformation circulating on social media and neighborhood gossip. Despite this, billions of people have received COVID-19 vaccines, saving over 20 million lives. But viral variants can still evade some of the immunity conferred by the original vaccines.[1] Future research should evaluate the long-term effects of vaccines, compare different vaccine types and vaccination programs, assess vaccine efficacy and safety in specific populations, and include outcomes related to persistent COVID-19.[1,2]

Nowadays, many experiments conducted by medical researchers have indicated that COVID-19 vaccines protect the population over 70 years old and reduce the risk of developing heart disease by 50 percent. It is known that the virus's capsid is composed of the S protein (Spike), which provides a mechanism for evading the host's immune system and can potentially cause heart disease. Specifically, the Spike protein targets cardiomyocytes (heart cells), especially in males, where a higher incidence has been observed. To understand the virus in general terms, let's imagine a chocolate bonbon filled with hazelnuts and a caramel center:

I. Spike Proteins (Hazelnuts): The spike proteins are like the hazelnuts in the bonbon. They are on the virus's surface and allow it to adhere to host cells. Each hazelnut represents a Spike protein that attaches to a cell.

II. Capsid (Chocolate Coating): The capsid is the protective layer surrounding the virus's genetic material. It's like the chocolate coating that envelops the entire bonbon, safeguarding the genetic material and helping the virus maintain its structure.

Genetic Material (Caramel Center): The caramel center in the bonbon represents the virus's genetic material. In the case of coronavirus, this genetic material is RNA (ribonucleic acid). It allows the virus to replicate within host cells (Figure 1).[1,2]
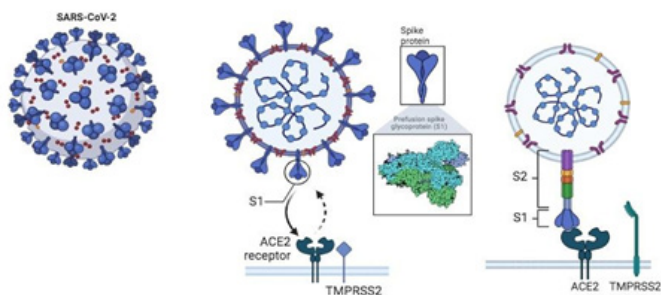

Figure 1 SARS-Covid with S protein Surface with ACE2 receptor. S protein is conformed by 3 identical units like circle organized, put up with ACE-2 receptor like a key mediated membrane covering fusion of virus with membrane host cell that is being infected. The S protein is activated through cellular protease TMPRSS2 located to closer from ACE-2.

The vascular pathology of SARS-CoV-2,[1] appears to be multifactorial, involving both direct effects of the virus and indirect effects from cytokine release. Let's break down the key points: Cytokines as Protectors: Cytokines (also known as citoquinas) act like soldiers protecting the immune system's headquarters (the immune response center) against any enemy attack (bacteria, viruses, or any agent that can cause infections and diseases). These proteins are released to defend the immune system from foreign invaders. The SARS-CoV-2 virus can induce an acute prothrombotic state. This state includes excessive coagulation (clotting), altered fibrinolysis (the process of dissolving clots), and sometimes endotheliopathy (dysfunction of blood vessel lining). Imagine this state as a house with pipes that begin to clog. If there's a sudden pressure variation, the pipes could break and cause havoc in the building. Endotheliopathy affects blood vessels' flexibility and stability. Think of blood vessels as flexible hoses. If the material (endothelium) is compromised, the hoses may deform, rupture, or lose stability. The virus's Spike protein plays a role in this process, potentially leading to heart disease by targeting cardiomyocytes (heart cells).[3,4] In summary, the interplay between cytokines, clotting, and endothelial health contributes to the complex vascular effects seen in COVID-19. Understanding these mechanisms is crucial for managing the disease and preventing complications.

When discussing fibrinolytic capacity, it refers to the ability to dissolve clots. Let's consider a dirty kitchen filled with grease: Fibrinolytic capacity acts as a solvent for that grease. If this capacity is impaired, more grease accumulates, making it difficult to clean the kitchen. Endotheliopathy refers to any disease related to blood vessels, affecting their vasodilation and constriction (changes in diameter). Let's imagine our veins as flexible hoses that change thickness based on water flow. The endothelium, like the material of the hose, separates the internal fluid from the external environment. If this material is compromised, it can lead to endotheliopathies causing dysfunction, imbalances, deformation, rupture, or compromised stability and durability of the vessel.[5]

Akhtar et al.[1] indicated that diagnostic and referral pathways for non-specific symptoms, such as dyspnea and fatigue, remain unclear. COVID-19 vaccination is generally cardioprotective, but is associated with myopericarditis in young men, although at a lower rate than after SARS-CoV-2 infection.[1] The goal of COVID-19 vaccines to prevent cardiovascular complications, including the potential long-term burden of COVID-19-related chronic cardiovascular diseases, is of clinical and public health importance. De Michelle et al[4] reviewed that those patients with a history of diabetes, ischemic stroke, and heart disease are at greater risk of developing this disease when patients are hospitalized with COVID-19; It is important to highlight that we do not have sufficient evidence to decide whether the direct cause of thrombotic events is related to vaccination after 1 or 2 doses of ChAdOx1-S (AstraZeneca) and BNT162b2 (Pfizer-BioNTech) especially in adults over 70 years of age. Hospital centers have a great problem of uncertainty: there is no exact way to carry out exhaustive monitoring of each and every patient, it is not possible to access the total information of each patient, as well as the treatments they have undergone. gone. subjected, previous pathologies and genetic predisposition. Precisely controlling multiple factors that can influence a thrombotic event, a cardiovascular accident or a heart attack makes it difficult to determine exactly whether it was really the vaccine that caused said event or the covid infection itself. Let us remember that many patients are asymptomatic.[5]

Barda et al.[7] studied the effect estimate was consistent with a potentially mild increase in the risk of Bell's palsy after vaccination, with a risk ratio of 1.32 (95% CI, 0.92 to 1.86). The absolute effect was small, with up to 8 excess events per 100,000 persons being highly compatible with our data according to the 95% confidence interval. Herpes zoster infection, the incidence of which we found to be increased after vaccination, is one of the potential causes of facial-nerve palsy.

An excessive risk of myocarditis (1 to 5 events per 100,000 people) (Table 2) was observed in association with the vaccine. Additionally, the risk of this potentially serious adverse event and other serious adverse events substantially increased after SARS-CoV-2 infection. This study was funded by the Ivan and Francesca Berkowitz Family Life Laboratory Collaboration at Harvard Medical School and the Clalit Research Institute. It is important to note that although the absolute number of observed myocarditis cases remains low, a higher risk was detected in those who received mRNA COVID-19 vaccines compared to unvaccinated individuals in the absence of SARS-CoV-2 infection. Given that mRNA COVID-19 vaccines are effective in preventing severe illness, hospitalizations, and deaths, future research should focus on accurately determining myocarditis rates related to these vaccines, understanding the biological mechanisms behind this rare cardiac event, and identifying those at higher risk.[7]

Table 2 Summary of the results from Barda et al.'s study

Adverse event	Risk ratio (RR)	Risk difference (RD)	Confidence interval (CI)
Myocarditis	3.24	2.7 events per 100,000 people	1.55 to 12.44
Lymphadenopathy	2.43	78.4 events per 100,000 people	2.05 to 2.78
Appendicitis	1.40	5.0 events per 100,000 people	1.02 to 2.01
Herpes zoster infection	1.43	15.8 events per 100,000 people	1.20 to 1.73
SARS-CoV-2 infection	18.28	11.0 events per 100,000 people	3.95 to 25.12

Infection rate and mortality rate were lower in vaccinated individuals irrespective of vaccine brand (Pfizer, Moderna, or Janssen). As of November 19, 2021, more than 448 million doses of the COVID-19 vaccine have been administered in The United States and during this time, VAERS has received 9810 reports of death (0.0022%) related to the COVID-19 vaccine. Reports of adverse events including mortality reports do not necessarily mean a vaccine-related complication. Total deaths from COVID-19 disease as of November 20, 2021 are more than 770461 in United States alone. Considering the risks and benefits of COVID-19 vaccines, it is evident that vaccines have a positive impact on COVID-19 related morbidity and mortality. Therefore, the CDC continues to recommend COVID-19 immunisation to all eligible individuals and continues to monitor upcoming data very closely.[8] The mRNA vaccines can also induce a non-specific innate inflammatory response or a molecular mimicry mechanism between the viral spike protein and an unknown cardiac protein. The other possibilities include the RNA in the vaccine itself, a potent immunogen, and produces bystander or adjuvant effect by cytokine activation of pre-existing autoreactive immune cells as young people usually have higher seroprevalence of SARS-CoV-2 even if they are asymptomatic during the COVID-19 pandemic. May can be use in the next years vaccine production, inoculated directly into human induced pluripotent stem cells-derived myocytes to study transcriptomic and morphological changes. It may help in understanding the mechanism of the mRNA vaccine-induced myocarditis or pericarditis.[9]

Many studies recognize the limitations, for example, they cite the possible bias when analyzing the samples, because patients usually report adverse effects when they already have a preconceived idea about them; while patients who thought the vaccines were safe showed no effects; which can be assumed to speak of a placebo effect. It should be noted that the sociocultural context, access to technology and the Internet, whether they live in rural and urban areas, age, and sex influence. Another important limitation to mention is the medical history of each patient and what previous pathologies they suffer from.[10]

Conclusion

In conclusion, the high risk of suffering a cardiovascular accident (blockage in blood flow to he heart) and an ischemic event (blockage/ hemorrhage in blood flow to the brain) is not related to the two. Although it is true that some patients admitted to hospital for SARS-Covid19 infection had a diagnosis during their admission and few patients underwent study. were detected on neuroimaging during hospital admission. So far we do not know exactly what the real reason why neurological and cardiovascular events appear, but many countries, such as Germany, have limited the age of AstraZeneca vaccination in adults over 60 years of age, the United Kingdom has limited the use of vaccines to people over 40 years of age and recommended ensuring protocols to improve the design of vaccines

with adenovirus vectors (Virus whose genetic material is DNA).

Despite this, to date, studies have shown that the risk of stroke and other pre-specified outcomes of interest (thrombocytopenia, venous thromboembolism, arterial thrombosis, CVST - Cerebral Venous Sinus Thrombosis - and myocardial infarction) after a SARS-CoV-2 infection were significantly higher than after vaccination with either the Oxford-AstraZeneca or Pfizer vaccines. As such, because the benefits of mass vaccination against COVID-19 far outweighed the risks of VITT (Coronavirus Vaccine-Induced Thrombosis), neither the European Medicines Agency nor the Food and Drug Administration found strictly conclusive data.[6] It is not clear what causes cardiovascular and cerebrovascular stroke, since in many cases patients present long COVID syndrome due to high levels of D-dimers that regulate blood coagulation.

From the studies by Adly and collaborators[11] it was considered that, although it is delimited in a geographical area, the tendency is that it is difficult to associate symptoms-causality- and if the pathologies are caused by covid per ce, if the Covid generates or is an activator as an interrupter of said pathologies and hence the cascade of adverse reactions, more studies are needed that are not biased, because it is seen that women tend to have adverse effects than men. It should be noted that data must be collected that are not biased by the same patient, because the majority after vaccination did not report any anomalies because these patients did not undergo hospitalization. One might also wonder about the post-vaccine effect that protects against hospitalization. In the Table 3, we can see that The Chi-square is 26.83, and the p-value is 0.0015. This suggests that there is a significant association between gender and adverse effects. By age: The Chi-square is 22.63, and the p-value is 0.0122. Here too, there is a significant association between age and adverse effects. It is important to consider other factors and continue investigating. Furthermore, the significant association in Chi-square tests could indicate that gender and age influence adverse effects. More concise data should continue to be investigated that includes patients who have been followed throughout the infectious process.

Table 3 Values Chi Cuadrado for Adly (2023).[11] Indicate significant associations between adverse effects and both gender and age. The low p-values suggest that these associations are unlikely to occur by chance

Group	Count	Non-hospitalized	Efficacy
Infected after 3 doses	237	234	-1.282051
Infected prior to vaccination	102	94	-8.510638
Uncertain infection in relation to vaccination	30	29	-3.448276

Additionally, here are the results of the Chi-square tests for adverse effects: **By Gender**: **Chi-square value**: *26.83* **p-value**: *0.0015.* **By Age**: **Chi-square value**: *22.63;* **p-value**: *0.0122.*

We must never forget prophylactic measures such as the use of a mask, hand washing and close monitoring of patients with immune pathologies, knowing that we must carry out routine examinations annually and monitor our vital signs if we suffer from risk diseases such as Type II Diabetes, hypertension, heart disease; It is part of individual health surveillance. However, we must keep in mind that data and its processing are a powerful tool, a meta-analysis must be carried out as a study to find out in context whether the variables and questions we ask ourselves 1) have answers and 2) these questions are well formulated and if it leads us to some hypothesis that we can test.

Acknowledgments

Conflicts of interest

The author declare that there are no conflicts of interest.

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