Review Article

Vaccination in cardiovascular prevention: a tool not always adequately appreciated

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ABSTRACT

Chronic coronary artery disease and heart failure remain leading causes of morbidity and mortality in Western countries. Beyond conventional treatments, complementary strategies such as vaccination have shown significant cardiovascular benefits. This narrative review explores the relationship between several vaccines—particularly those for influenza, SARS-CoV-2, pneumococcus, and herpes zoster—and the prevention of cardiovascular and cerebrovascular events, both in primary and secondary prevention contexts. The pathophysiological mechanisms linking respiratory infections to acute events such as myocardial infarction and stroke are analyzed, as well as clinical evidence supporting vaccine use in patients with preexisting cardiovascular disease. Adverse effects, though rare, are also discussed, given their disproportionate media and scientific attention. Additionally, the article addresses vaccine hesitancy, examining its sociocultural determinants and emphasizing the crucial role of healthcare professionals in counteracting misinformation through education and strong patient-provider relationships. Overall, vaccination emerges not only as an essential tool for preventing infectious diseases, but also as an effective strategy to reduce the cardiovascular burden in high-risk populations.

INTRODUCTION

Chronic coronary artery disease (CAD) and heart failure are still the main mortality causes in Western countries. In spite of advancements in the standardized treatment of both conditions and a reduction in attributable mortality of up to 25% in the last decade, new supplementary strategies have emerged, not directly related with cardiovascular physiology, but proving to have a positive impact on the comprehensive management of these patients. Between these strategies, the administration of several vaccinations stand out. They not only protect vulnerable patients from the severe consequences of preventable infectious diseases, but as we will see, they are also associated to a reduction in the incidence of acute myocardial infarction (AMI).[1,2] This narrative review is focused on the impact of vaccination on the development of CAD, as well as its role in the protection of individuals with cardiovascular disease.

RELATIONSHIP BETWEEN VACCINE-PREVENTABLE DISEASES AND CARDIOVASCULAR HEALTH

Since the end of the 1970s, there is experimental evidence linking certain viruses, particularly the herpes zoster virus, with the development of atherosclerotic disease in animal models.[3] Later, epidemiological observations, such as the seasonal increase in mortality by cardiovascular cause during the winter months in cold regions of Europe, as well as the identification of procoagulant factors associated to AMI, established the foundations to research the relationship between infectious diseases and the subsequent cardiovascular disease.[4,5]

Already in the 21st century, the FLUVACS study showed that vaccination against influenza can reduce mortality in up to 75% in 6 months and close to 50% of the combination of mortality, reinfarction and readmission by ischemia in post-AMI patients or who have undergone elective angioplasty, in comparison with non-vaccinated individuals.[6]

Since year 2006, the American Heart Association supports and promotes the yearly vaccination against influenza in patients with preexisting cardiovascular disease, based on evidence from cohort studies and randomized clinical trials.[7] This recommendation is aimed at reducing both cardiovascular morbidity and general mortality in this vulnerable population.

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EFFICACY OF VACCINES IN THE PREVENTION OF CARDIOVASCULAR DISEASES

To understand the protective effects of certain vaccines on cardiovascular diseases, it is essential to analyze the pathophysiological relationship between vaccine-preventable infections and cardiovascular system compromise.

In general terms, severe respiratory infections are usually accompanied by fever, hypoxemia and exacerbated adrenergic response, particularly in the presence of septic syndrome. These factors may trigger myocardial ischemia by increase in oxygen demand, originating type 2 AMI. Furthermore, the systemic inflammatory response, mediated by proinflammatory cytokines and procoagulant factors, favoring endothelial dysfunction and thrombi formation. Interleukins such as IL-1b, IL-6 and tumor necrosis factor alpha (TNFa) have proatherogenic effects, promoting neutrophil and monocyte infiltration within atherosclerotic plaques, which accelerates its progression and may trigger type 1 AMI.

On the other hand, the direct viral replication in cardiomyocytes may trigger myocarditis, ventricular arrhythmias and contractile failure. Likewise, in patients with chronic CAD, the macrophages present in plaques may suppress helper T lymphocyte activity, weakening antiviral immune response.[8]

In the specific case of the vaccine against influenza, numerous observational studies and meta-analysis have shown a decrease in mortality in patients with heart failure with reduced ejection fraction (<40%). Although no randomized studies have been carried out in this subgroup, indeed there is sound evidence, both from controlled and randomized studies, backing its efficacy for primary prevention of AMI.[8] In post-AMI patients, the administration of vaccination up to 72 hours after the event has shown to reduce all-cause mortality by 28%, as well as the incidence of new AMI and stent thrombosis up to a year after the event.[8] Flu vaccines have also been associated to less incidence and severity of cerebrovascular diseases (CVD), as well as a reduction in risk of hospital admission.[8]

As to pneumococcus (Streptococcus Pneumoniae), the relationship with cardiovascular disease is bidirectional: the presence of cardiovascular disease worsens the evolution of pneumonia, and in turn, this is associated to a greater risk of acute coronary syndrome (OR 3.02), CVD (OR 2.88) and mortality (3.22) in patients with acute community-acquired pneumonia. Pneumococcal vaccination (whether by the sequential scheme of 13 and 23 serotypes, or with a conjugate vaccine of 20 serotypes) is indicated in people older than 65 years, as well as in patients with immunodeficiency, cerebrospinal fluid fistulae or cochlear implants.[9] A prospective study that evaluated the combined vaccination against influenza and pneumococcus reported significant reductions in mortality (35%), CVD (33%), AMI (48%) and acute pneumonia (43%).[8] Other studies also have shown relevant decreases in the rate of hospitalization due to heart failure and other causes between patients vaccinated for pneumococcus.

Around 20% of admitted patients with infection by SARS-CoV-2 virus, the agent causing COVID-19, have shown biochemical evidence of myocardial compromise and increase in mortality. The heterogeneity of the presentation in several forms of the disease makes it difficult to obtain accurate data on the real incidence of cardiovascular compromise in COVID-19. However, it is known that, in cohorts in the United States, where vaccination predominates with vaccines mediated by messenger RNA, partial and full immunization are associated to an increasingly less incidence of major cardiovascular events.[8,10]

Also, a growing interest has been observed on the respiratory syncytial virus (RSV) impact, including hospitalization and death, particularly in patients with preexisting cardiovascular conditions. Just as with influenza in past decades, yearly peaks of infection by RSV coincide with a greater number of cases of first AMI, recurrent AMI and CVD. However, the new vaccines against RSV, that reduce the incidence of pulmonary infection, have not yet proven a protective effect before cardiovascular complications.[8,11]

Finally, a systematic review researched the efficacy of the vaccine against herpes zoster in prevention of infarction, heart failure, major cardiovascular and cerebrovascular events, having found only two studies were a reduction close to 12% was proven in the incidence of CVD, or of 50% in the report of new CVDs between vaccinated people older than 65 years.[12]

ADVERSE EFFECTS OF VACCINES USED IN PATIENTS WITH CARDIOVASCULAR DISEASES

Vaccines represent, after access to drinkable water, the most effective public health strategy to reduce morbidity and mortality associated to infectious diseases. Since mid-20th C, multiple vaccines have been developed and widely used: the vaccine against tetanus, diphtheria and whooping cough started to be used in 1940, with its acellular formulation (DTPa) being introduced in 2005; flu vaccines have been applied since the same decade; and the MMR vaccine (measles, mumps and rubella) has been available in its current version since 1971. More recently, vaccines against SARS-CoV-2 were authorized to be used between the end of 2020 and the beginning of 2021.

In spite of the overwhelming evidence on the efficacy of these vaccinations, the public and scientific focus have often focused on their adverse effects, some of which (although rare) have generated concern due to their severity or media impact. In the United States, the VAERS (Vaccine Adverse Event Reporting System) allows any person (health care professionals, patients, carers, educators or manufacturers) to report possible adverse events associated to vaccination (https://vaers.hhs.gov). From the existing documents in this database, or the systematic study of cases and cohorts, it is known now that the adverse cardiovascular effects of vaccines are scarce and essentially limited to cases of myocarditis and pericarditis.[8,13]

We should highlight that establishing a causal relationship between a vaccine and a specific adverse effect is complex in epidemiological studies, due to the lack of mechanistic information that would allow confirming such connection. Instead, case reports and clinical series may contribute more clarity when there are criteria backing causality: a well-defined time association, pathophysiological evidence obtained from experimental models and, if possible, the reproducibility of the adverse effect after a new exposition to the vaccination agent.[14]

Within this framework, a recent systematic review gathered reports and series of patients who experienced cardiovascular events after vaccination, whose findings are summarized in *Table 1*.[13]

On the other hand, a rare syndrome has been described, characterized by thrombocytopenia and thrombosis (frequently with dural venous sinuses compromise) in association with vaccines against SARS-CoV-2 that use adenoviral vectors, as those developed by AstraZeneca and Johnson & Johnson.[8] Although these events are very rare, their early detection has enabled establishing specific protocols for diagnosis and treatment, minimizing their clinical impact.

TABLE 1.
Case reports of cardiovascular compromise after vaccination

Type of vaccine	Number of studies	Number of cases	Manifestation
Influenza	11	34	Myocarditis (2) Pericarditis (27) Pericardial effusion (2) Takotsubo (2) Kounis syndrome (1)
COVID subtype **J&J: 1** **Pfizer: 35** **Moderna: 26** **Covishield: 4** **CoronaVac: 1**	18	67	Myocarditis (55) AMI (7) Kounis syndrome (1) MINOCA (1) Pericarditis (2)
Smallpox	20	232	Myocarditis (75)Pericarditis (7)Myopericarditis (121) Ischemia (26) Dilated cardiomyopathy (2) Trigeminy (1) Ventricular tachycardia (1)
Pneumococcus	2	2	Myocarditis (1) Pericardial effusion (1)
Tetanus	3	3	Myocarditis (2) Myopericarditis (1)
Cholera	1	1	AMI (1)

RESISTANCE TO VACCINES AND HOW TO APPROACH IT

Beyond the specific disease they prevent, of their efficacy, safety profile and administration access, vaccines may be classified in a pragmatic way in two large groups: those that provide individual protection (such as vaccines against tetanus and rabies) and those that offer community protection (such as measles, influenza and COVID-19). In scenarios of outbreaks, epidemics or pandemics, a collective solidarity sense emerges, where individuals understand that their decision to get a vaccine can benefit the whole community.

In the cardiovascular field, only vaccines against SARS-CoV-2 and influenza have proven to provide benefits both at individual and community levels.

In 2019, the World Health Organization identified the hesitation before vaccines as one of the ten main threats to global health.[15] Since the publication (and subsequent recantation) of the infamous article in The Lancet in 1998, linking the MMR vaccine (measles, mumps and rubella) to autism, mistaken concepts on vaccination have spread, generating unfounded doubts in the population. In epidemiology, it is taught that the absence of evidence does not necessarily entail evidence of absence; however, multiple studies have refuted the most common beliefs against vaccines, such as saturating the immune system, inducing autoimmune diseases or negatively affecting the course of pregnancy.[15]

Although it is not completely clear if the attitude by parents before child vaccination predicts their behavior in regard to their own immunization, research in the United States, Canada and the United Kingdom has identified certain factors associated to further hesitation: young parents, lower educational level, strong religiousness and low trust in health care professionals.[16] Different studies also have observed that people with no strong stance (either in favor or against) are susceptible to the influence of public figures, whether physicians, politicians or celebrities, which may lead them to modify their decisions on vaccination.[17,18,19,20,21] In turn, excess of information in social networks, with no effective mechanisms for verification, not just feeds doubts, but may generate paralysis before decision-making.[22]

These observations underscore the critical role that health care professionals play, whatever their specialties, at the time of advising their patients. Scientific evidence, persistence by physicians and the quality of doctor-patient relationships are fundamental elements to encourage vaccination, and thus, protecting both individuals and communities.

CONCLUSIONS

Vaccination against influenza, SARS-CoV-2 and pneumococcus is associated to cardiovascular protection by mechanisms independent from cardiovascular physiology. The vaccine against herpes zoster would have a protective role against cerebrovascular disease. Although other vaccines do not directly reduce cardiovascular or cerebrovascular risk, patients with these comorbidities are particularly vulnerable to severe forms of preventable infectious diseases. In this scenario, vaccination consolidates as an essential tool to protect this population from risk.

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