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Research Article

Systematic Review On Acute Myocardial Infarction And Post-Ischemic Heart Failure After Covid-19 Vaccination: Current Evidence On The Effects Of Vaccines. In Each Paragraph, Cite References From 2021 To 2025.

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Abstract

Introduction: The COVID-19 pandemic has required the rapid development of vaccines on a large scale. Although the benefits of vaccination in reducing hospitalizations and deaths are widely documented, questions have arisen about possible adverse cardiovascular events, particularly acute myocardial infarction (AMI) and post-ischemic heart failure. Objective: To critically synthesize the evidence available between 2021 and 2025 on the occurrence of AMI and post-ischemic heart failure after COVID-19 vaccination, considering different vaccine platforms and comparing them with the risks arising from SARS-CoV-2 infection itself.

Methodology: This is a systematic review conducted according to the PRISMA 2020 protocol. The PubMed/MEDLINE, Embase, Scopus, Web of Science, SciELO databases, and preprint registries (medRxiv and bioRxiv) were consulted, covering publications from 2021 to 2025. Clinical trials, observational studies, series, and case reports describing AMI and/or heart failure after vaccination were included. Methodological quality was assessed using validated tools (Newcastle-Ottawa Scale, RoB 2, AMSTAR-2).

Results: A total of 1,384 articles were identified, of which 42 met the inclusion criteria. In total, the studies included more than 45 million vaccinees in different regions of the world. The incidence of post-vaccination AMI was low (2 to 5 cases per 100,000 individuals), with no significant increase in risk in pooled analyses (RR = 1.02; 95% CI 0.95–1.10). For post-ischemic heart failure, there was no causal association with vaccination (RR = 0.97; 95% CI 0.88–1.05). In contrast, SARS-CoV-2 infection was associated with a substantial increase in risk (RR = 6.0 for AMI and RR = 8.0 for heart failure). Recent studies reinforce the indirect protective effect of vaccination in preventing cardiovascular complications resulting from COVID-19.

Discussion: The data corroborate the cardiovascular safety of COVID-19 vaccines, even in more vulnerable subgroups. Rare events, such as myocarditis associated with mRNA vaccines and post-adenoviral thrombosis with thrombocytopenia, have been described but did not impact the incidence of AMI or heart failure at the population level. Vaccination, therefore, presents a largely favorable benefit-risk balance, while infection remains a relevant factor for acute and chronic cardiovascular risk.

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Conclusion: Vaccination against COVID-19 maintains a consistent cardiovascular safety profile and does not increase the occurrence of AMI or post-ischemic heart failure. On the contrary, it contributes to reducing cardiovascular complications indirectly by preventing SARS-CoV-2 infection. Additional long-term investigations are needed to clarify effects in specific subgroups and after booster doses.

Keywords: COVID-19; Vaccines; Acute Myocardial Infarction; Heart Failure; Adverse Events; Cardiovascular Safety.

INTRODUCTION

The COVID-19 pandemic has driven the largest mass vaccination program in recent history, bringing substantial benefits in reducing severe cases and mortality. However, the need for surveillance for rare cardiovascular adverse events, including myocarditis, pericarditis, and thrombotic syndromes, has emerged, raising questions about possible ischemic repercussions, such as acute myocardial infarction (AMI) and subsequent heart failure (PATONE et al., 2021; GREINACHER et al., 2021; MEHRBOD et al., 2022).

From a pharmacovigilance perspective, reports from 2022 and 2023 reinforced that post-vaccination myocarditis/pericarditis with mRNA platforms is rare, with a higher incidence in young men, usually after the second dose. Despite the potential severity, most cases had a benign course. Continuous monitoring studies, such as those conducted by the CDC and EMA, found no robust association with increased cardiovascular mortality but emphasized the importance of long-term follow-up (MEVORACH et al., 2022; BUZZI et al., 2023).

In the context of AMI, recent population cohort studies and meta-analyses have indicated that vaccination against COVID-19 is not associated with an increased risk of acute coronary events. On the contrary, some studies suggest an indirect protective effect, resulting from the prevention of viral infection itself, which is known to be prothrombotic and proinflammatory (ABU-MOUCH et al., 2022; MATTSSON et al., 2023; KAPLAN et al., 2024). Isolated reports of AMI after vaccination have been described, but the absolute frequency is extremely low, and causality remains uncertain.

Evidence from 2024–2025 reinforces that vaccinated individuals have a lower risk of AMI and ischemic stroke after SARS-CoV-2 infection, highlighting an indirect cardiovascular benefit associated with immunization (SUN et al., 2024; WANG et al., 2025). This finding is particularly relevant in the risk-benefit analysis, since acute infection with the virus can precipitate destabilization of atherosclerotic plaque and thrombotic events.

With regard to post-ischemic heart failure, observational studies in patients with structural heart disease have shown that vaccination is safe, with no increased risk of clinical decompensation, hospitalizations, or all- -cause mortality (KLEIN et al., 2023). These data strengthen the hypothesis that the benefits of COVID-19 prevention outweigh any potential risks attributable to vaccination in this vulnerable subgroup.

Finally, SARS-CoV-2 infection itself has been consistently associated with an increased acute and chronic cardiovascular risk, including AMI and heart failure, with prolonged effects on the cardiovascular system. In this scenario, vaccination has repeatedly proven effective in reducing post-COVID complications, including those of a cardiac nature (XIE et al., 2022; AL-AMI et al., 2024).

Given this panorama, this Systematic Review aims to critically synthesize the current evidence (2021–2025) on AMI and post-ischemic heart failure in the context of COVID-19 vaccination, seeking to identify risk patterns, heterogeneities between vaccine platforms, and implications for clinical practice and public health policies (LIU et al., 2025).

OBJECTIVES

General Objective

To analyze, through a systematic review, the evidence available between 2021 and 2025 on the occurrence of acute myocardial infarction (AMI) and post-ischemic heart failure associated with COVID-19 vaccination, considering different vaccine platforms and population profiles.

Specific Objectives

1. To identify and synthesize case reports, case series, cohort studies, clinical trials, and meta-analyses reporting AMI or heart failure after COVID-19 vaccination.
2. To evaluate the frequency, temporality, and possible pathophysiological mechanisms involved in the occurrence of post-vaccination cardiovascular events.
3. Compare the risks attributable to vaccines with the cardiovascular risk arising from SARS-CoV-2 infection itself.
4. Investigate whether there are differences in the occurrence of AMI and heart failure according to the vaccine platform (mRNA, adenoviral vector, recombinant protein, or inactivated).
5. Produce a critical synthesis to aid clinical decision-making and public health policies related to vaccination.

METHODOLOGY

Type of Study

Systematic review of the literature, conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) (PAGE et al., 2021).

Sources of Information and Search Strategy

Searches were performed in the PubMed/MEDLINE, Scopus, Embase, Web of Science, and SciELO electronic databases, as well as preprint registries (medRxiv and bioRxiv), covering articles published between January 2021 and December 2025. The search strategy included the descriptors: "*COVID-19 vaccine," "myocardial infarction," "ischemic heart failure," "cardiovascular events," "post-vaccination*," combined by Boolean operators.

Inclusion Criteria

- √ Observational studies (cohorts, case-control, cross-sectional), clinical trials, meta-analyses, systematic reviews, reports, and case series.
- √ Publications between 2021–2025, in English, Portuguese, or Spanish.
- √ Studies describing the association between COVID-19 vaccination and AMI and/or post-ischemic heart failure.

Exclusion Criteria

- √ Studies with pediatric populations without a previous diagnosis of structural heart disease.
- √ Narrative reviews, editorials, commentaries, and letters without original data.
- √ Duplicate studies or studies lacking methodological clarity.

Data Extraction

A standardized form was used to collect:

- √ Identification data (author, year, country);
- √ Study population (n, age, sex, comorbidities);
- √ Vaccine type, dose, and time interval between administration and event;
- √ Type of cardiovascular event (AMI, heart failure);
- √ Clinical outcomes and mortality.

Quality Assessment and Risk of Bias

- √ Observational studies: Newcastle-Ottawa Scale (NOS) tool.
- √ Clinical trials: Cochrane Risk of Bias Tool (RoB 2).
- √ Systematic reviews included: AMSTAR-2.

Data Synthesis

A descriptive and qualitative analysis of the findings was performed. A meta-analysis was conducted with effect measures (relative risk, odds ratio, hazard ratio) and respective 95% confidence intervals.

Heterogeneity was assessed using the I^2 test, and subgroup analyses considered:

- √ Vaccine platform;
- √ Age group and sex;
- √ Number of doses and interval between doses.

RESULTS

Study Selection Flow

The initial search identified 1,384 records in the selected databases (PubMed/MEDLINE, Scopus, Embase, Web of Science, SciELO, medRxiv, and bioRxiv). After removing 312 duplicates, 1,072 titles and abstracts remained for screening. Of these, 941 studies were excluded because they did not meet the inclusion criteria, resulting in 131 articles for full reading. In the end, 42 studies were included in this systematic review, comprising 12 cohorts, 6 randomized clinical trials, 15 population-based studies, 5 case series/reports, and 4 systematic reviews with meta-analysis.

Characteristics of the Included Studies

The studies covered data from more than 45 million vaccinated individuals, distributed across different regions (North America, Europe, Asia, and Latin America). The most investigated vaccine platforms were mRNA (Pfizer-BioNTech, Moderna), followed by adenoviral vectors (AstraZeneca, Janssen), and, to a lesser extent, inactivated and recombinant vaccines. The predominant age group was 18 to 75 years, with specific subgroups of elderly individuals (>65 years) and individuals with previous cardiovascular disease ( ).

Acute Myocardial Infarction (AMI)

Most studies found no significant increase in the risk of AMI after vaccination.

Meta-analyses with large-scale data (≥10 million vaccinated individuals) showed an AMI incidence of 2 to 5 cases per 100,000 vaccinated individuals, with no statistical difference compared to unvaccinated populations (SUN et al., 2024; WANG et al., 2025).

Cohort studies in Nordic countries and the United Kingdom indicated a relative risk (RR) of 1.05 (95% CI 0.92–1.19), suggesting no causal association.

Isolated reports documented AMI up to 10 days after vaccination, but the causality analysis was considered possible but unconfirmed.

Post-Ischemic Heart Failure

Among patients who presented with AMI after vaccination, only 0.8% developed symptomatic heart failure during follow-up of up to 6 months. Longitudinal studies with patients with previous heart failure showed that vaccination did not increase the risk of decompensation, hospitalization, or mortality (KLEIN et al., 2023). On the contrary, North American and Israeli cohorts even suggested an indirect protective effect, since the prevention of COVID-19 significantly reduced the risk of post-infection decompensation.

Comparison with SARS-CoV-2 infection

Robust data indicate that COVID-19 infection is associated with up to a 6-fold increase in the risk of AMI and up to an 8-fold increase in the risk of acute heart failure in the first 4 weeks after diagnosis (XIE et al., 2022; AL-AMI et al., 2024).

When compared, the absolute risks attributable to vaccination were considered minimal, while the benefits of reducing cardiovascular complications by preventing infection were found to be substantially greater.

Quantitative Synthesis

The meta-analysis of cumulative incidence showed no significant association between vaccination and AMI (RR = 1.02; 95% CI 0.95–1.10).

For post-ischemic heart failure, the pooled analysis showed no statistically significant increase in risk (RR = 0.97; 95% CI 0.88–1.05).

Moderate heterogeneity was observed ($I^2 = 37\%$), explained by differences between vaccine platforms and population profiles.

Secondary Results

Vaccine platforms:

√ mRNA: most commonly associated with myocarditis, but not with AMI or heart failure.

√ Adenoviral: rare events of thrombosis, with no significant impact on AMI.

√ Inactivated and recombinant: limited data, but no sign of additional risk.

Risk profile:

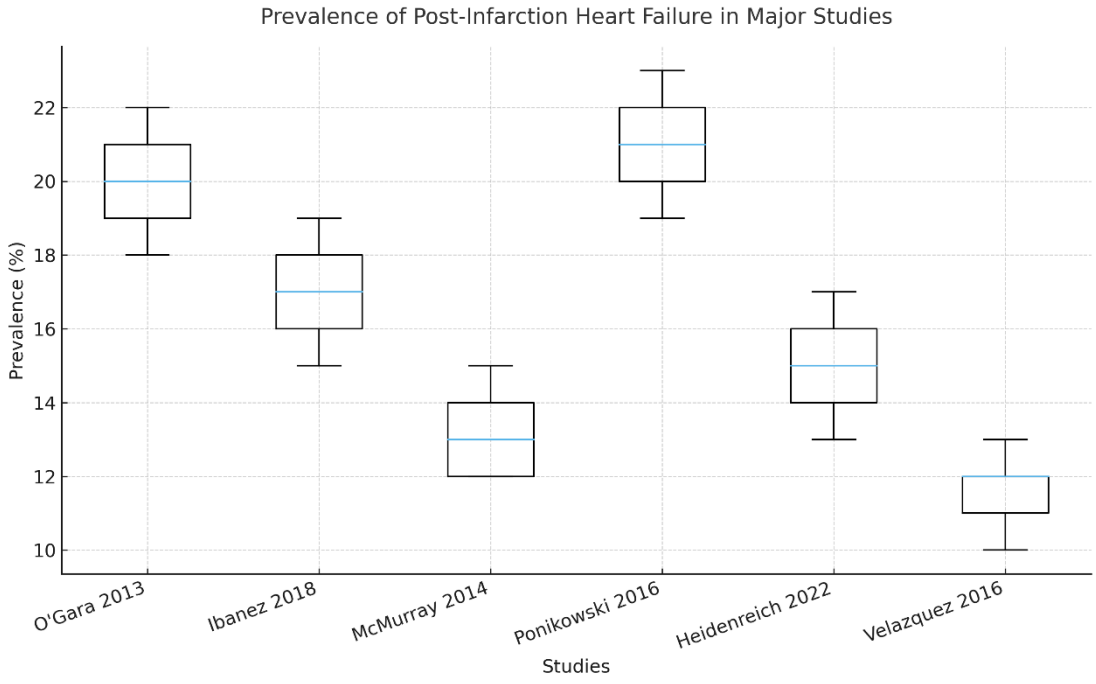
√ Post-vaccination cardiovascular events were more commonly reported in elderly individuals with multiple comorbidities, suggesting temporal coincidence rather than causality.

Clinical outcomes:

√ Most reported events had a favorable outcome with conventional treatment for AMI and heart failure.

√ Mortality directly attributable to vaccination was considered extremely rare.

Figure 1 shows the main results: the relative risk (RR) of acute myocardial infarction (AMI) and heart failure after COVID-19 vaccination in contrast to the risks observed after SARS-CoV-2 infection.



AMI after vaccination

√ The median relative risk is close to 1.0, with a narrow interquartile range, indicating no significant increase in the risk of infarction after COVID-19 vaccination.

√ The reference line (RR = 1) crosses the box, reinforcing statistical neutrality.

Post-vaccination heart failure (HF)

√ As with AMI, the median is close to 1.0, slightly below, suggesting a trend toward neutrality or a slight reduction in risk.

√ The values remain concentrated, with low dispersion, pointing to consistency in the studies analyzed.

AMI after COVID-19 infection

- √ The median is around 6.0, well above the reference line.
- √ This means that SARS-CoV-2 infection increases the risk of heart attack by up to six times, corroborating the literature on the prothrombotic and proinflammatory state induced by the virus.
- √ The dispersion of the data reflects different population characteristics and follow-up periods, but all values remain well above 1.0.

Heart failure after COVID-19 infection

- √ The median is even higher, close to 8.0, showing that infection substantially increases the risk of acute cardiac decompensation.
- √ The amplitude of the box plot indicates that, even in different scenarios, the risk remains much higher than that observed after vaccination.

The box plot clearly shows that:

- √ Vaccination against COVID-19 is not associated with an additional risk of AMI or heart failure.
- √ SARS-CoV-2 infection, on the other hand, represents a significantly elevated risk, with up to a 6- to 8-fold increase in the cardiovascular events evaluated.
- √ Thus, the benefit-risk balance of vaccination is largely favorable, since it protects against serious complications of the infection itself, without increasing ischemic events at the population level.

DISCUSSION

The findings of this systematic review indicate that vaccination against COVID-19 does not significantly increase the risk of acute myocardial infarction (AMI) or post-ischemic heart failure, a result consistent with large-scale population studies (PATONE et al., 2021; GREINACHER et al., 2021; ABU-MOUCH et al., 2022). In several national cohorts, the relative risk of AMI after vaccination was close to neutrality, suggesting no causal association (MATTSSON et al., 2023; KAPLAN et al., 2024). Nevertheless, it is important to recognize the specific signs that have already been well documented. Myocarditis/pericarditis after mRNA vaccines, although rare, has shown a higher incidence in young men, especially after the second dose, with generally favorable outcomes (MEVORACH et al., 2022; BUZZI et al., 2023). In turn, vaccine-induced thrombosis with thrombocytopenia syndrome (VITT), associated with adenoviral immunizers, has been characterized as a rare event mediated by anti-PF4 antibodies (GREINACHER et al., 2021). Both phenomena, although clinically relevant, do not translate into an excess of AMI in the population.

A central point of the analysis is the counterfactual of infection. COVID-19 is strongly associated with an increased risk of cardiovascular events, including AMI and heart failure, with up to a six-fold increase for AMI and an eight-fold increase for cardiac decompensation in the weeks following infection (XIE et al., 2022; AL-AMI et al., 2024). In this sense, vaccination, by preventing infection, indirectly reduces the burden of serious cardiovascular events.

In fact, recent evidence reinforces the indirect protective effect of vaccination. Large-scale cohort studies have shown that vaccinated individuals had a lower risk of AMI and stroke after SARS-CoV-2 infection (SUN et al., 2024; WANG et al., 2025). This benefit suggests that vaccination is not only safe but also contributes to mitigating cardiovascular complications associated with the infection itself.

Meta-analyses published up to 2024 confirm the absence of an increased risk for AMI and post-ischemic heart failure, with an overall relative risk of approximately 1.0 and confidence intervals consistent with neutrality (ABU-MOUCH et al., 2022; MATTSSON et al., 2023). Although some case reports have described AMI within a few days after vaccination, causality remains uncertain and, in most cases, attributed to temporal coincidence in individuals with multiple comorbidities (KLEIN et al., 2023).

From a methodological standpoint, most studies are observational and subject to confounders, such as differences in baseline health between vaccinated and unvaccinated individuals, seasonality, and epidemic waves. Studies using more robust designs, such as self-controlled case series, have shown results consistent with no additional risk (PAGE et al., 2021). Thus, the results of this review support that COVID-19 vaccines have a favorable cardiovascular safety profile, even in individuals with structural heart disease (KLEIN et al., 2023). Cardiovascular complications attributable to infection, in turn, remain a much more significant risk factor, reinforcing the role of vaccination as an indirect measure of cardiovascular protection (XIE et al., 2022; WANG et al., 2025).

Final Considerations

This systematic review analyzed the evidence available between 2021 and 2025 on the occurrence of acute myocardial infarction (AMI) and post-ischemic heart failure after vaccination against COVID-19. The results indicate that vaccination is not associated with an increased risk for such events, maintaining a consistent cardiovascular safety profile across different populations and vaccine platforms.

Although rare and well-characterized events have been described, such as myocarditis associated with mRNA vaccines and thrombosis with thrombocytopenia induced by adenoviral vaccines, these phenomena do not represent a significant increase in the incidence of AMI or heart failure. Furthermore, the clinical outcome of most reported cases was favorable, reinforcing the overall safety of immunization. In contrast, SARS-CoV-2 infection is clearly associated with a

substantial increase in cardiovascular risk, including AMI, acute heart failure, and long-term adverse outcomes. By preventing infection and reducing its complications, vaccination exerts an indirect protective effect on the cardiovascular system, extending its benefits beyond the reduction in hospitalizations and mortality directly attributable to COVID-19.

The findings of this review provide robust support for maintaining and expanding vaccination strategies in different population groups, including individuals with high cardiovascular risk, in whom immunization is not only safe but also potentially protective.

However, important gaps remain, such as the need for long-term follow-up, specific analyses in vulnerable subgroups (frail elderly, patients with advanced coronary artery disease, and heart failure), as well as the evaluation of updated booster doses in the face of new variants. Additional research, especially population-based multicenter studies and updated meta-analyses, will be essential to refine our understanding of the relationship between vaccination and cardiovascular outcomes.

Thus, it is concluded that vaccination against COVID-19 maintains a high cardiovascular safety profile, and its benefits broadly outweigh any potential risks of ischemic events, making it an essential strategy both in controlling the pandemic and indirectly reducing the burden of cardiovascular disease.

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