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Myocardial Infarction Following Vaccination Against COVID-19: A Systematic Review

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Abstract

Context: Several reports have been presented regarding the occurrence of acute myocardial infarction following vaccination against COVID-19.

Objectives: The current systemic review tried to review and summarize the published evidence and documents regarding the occurrence of myocardial infarction following various types of anti-COVID-19 vaccines (AstraZeneca and Pfizer) and, finally, take steps to clarify the causes of such incidents.

Methods: The relevant databases, including Medline, Web of Knowledge, Google Scholar, Scopus, and Cochrane, were comprehensively searched by the two blinded researchers for all eligible studies based on the considered keywords. Of 76 articles initially collected by database searching, 20 articles were included in the last analysis.

Results: The occurrence of acute myocardial infarction was mostly related to SARS-CoV-2-based messenger RNA and viral vector vaccines. This cardiac attack occurred after the first vaccination in 74% of patients affected. The time of occurrence of myocardial infarction was also very different between different types of vaccines and varied between 15 minutes and 21 days after vaccination. Most of the myocardial infarctions that occurred after vaccination were of the ST-segment elevation type (STEMI) (23 of 28 patients). More than two-thirds of myocardial infarction cases occurred in patients who had significant cardiovascular risk profiles (hypertension, diabetes mellitus, and ischemic heart disease). Overall, 22.2% of cases suffering post-vaccination myocardial infarction died within hospitalization.

Conclusions: The occurrence of myocardial infarction following the vaccination against COVID-19 is rare, and due to the fatality of this event, it is necessary to modify the biotechnological production of existing vaccines and to accurately evaluate the pathophysiology of this event.

Keywords: Myocardial Infarction, COVID-19, Vaccine, Atherosclerosis, Virus

1. Context

With the emergence of the COVID-19 pandemic and the subsequent published statistics of its significant morbidity and mortality from the very first months of the onset of the disease, the efforts of researchers and medical staff were directed to reduce the severity of the disease by providing effective treatment protocols, developing written guidelines for the care of patients, and also the preparation of effective vaccines to prevent the occurrence of disease and its severity (1, 2). In less than two years after contracting this disease, effective vaccines against the disease-causing virus of various types of killed virus, weakened virus or using the virus genome were prepared and offered commercially, which resulted in their use in almost all human societies and led to limiting the mortality of patients, reducing the successive waves of the disease, and successfully controlling the complications of the disease (3-5). However, since the use of these vaccines, reports of their significant side effects have been published, both early and delayed, and some of these side effects were sometimes associated with morbidity and even mortality of patients (6). Annoying headaches, thromboembolic events, cerebrovascular events, and even ischemic heart disease and acute myocardial infarction have been potential side effects reported following the use of these types of vaccines. Even in some cases, especially cardiac ischemic events, no specific traces were found for the pathophysiological interpretation of these results

(7). Sometimes, the occurrence of myocardial infarction within the first 24 hours after the injection of the vaccine in patients who had no history of cardiovascular diseases or their underlying risk factors was predictable (8). Some researchers believe that the cause of such a heart complication is the direct invasion of the virus into the myocardial tissue and its penetration through specific receptors (ACE II) located in the myocardium, resulting in the occurrence of myocarditis and cardiomyopathy (9). Some consider the coronary vessels as the direct target tissue of the virus and as a result of damage to the vascular wall, endothelial dysfunction, formation of atherosclerotic plaque, and, therefore, coronary artery stenosis and cutting (10). However, the reasons for the occurrence of such acute vascular events are still unclear, and its exact pathophysiology is still uncertain. In addition, the published reports have been limited mainly in the form of case reports of patients.

2. Objectives

The current systemic review tried to review and summarize the published evidence and documents regarding the occurrence of myocardial infarction following various types of anti-COVID-19 vaccines and, finally, take steps to clarify the causes of such incidents.

3. Materials and Methods

We planned the current systematic review based on the guidelines for the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) (11). First, the study questions and suggestions were developed, including "What is the prevalence of myocardial infarction following the use of COVID-19 vaccination?" "Which types of vaccines have been associated with a higher risk of this complication?" "What was the time interval between the vaccination and the occurrence of this event?" and "What could be the possible mechanism of this cardiovascular accident?" In the next step, the relevant article databases, including Medline, Web of Knowledge, Google Scholar, Scopus, and Cochrane, were comprehensively searched by the two blinded researchers for all eligible studies based on the considered keywords of "COVID-19", "vaccine", "prevalence", "myocardial infarction", "coronary artery", "atherosclerosis", "virus", and "myocarditis". Resolving disagreements was achieved by reaching a consensus between the parties involved or by seeking the assistance of a neutral third party. To retrieve the studies, the inclusion criteria were taken into consideration.: (1) the studies finally assessed were those described the cases who had no previous history of cardiovascular disease or underlying disorder risk profiles that suffered myocardial infarction following the inoculation of the COVID-19 vaccine; (2) the studies were restricted to the English language unless it was possible to translate the original version of the article completely and fluently; (3) the studies with unclear or irreproducible results were all excluded; (4) full manuscript access was needed, unless abstract data are sufficient for analysis or the full text of the article was provided by sending an email and requesting to release it; (5) any related review articles were also excluded from the study. As shown in the study selection flow diagram (Figure 1), at first, the database search yielded 76 articles. After identifying three duplicated articles, 73 records were primarily under-screened. Through the evaluation of the titles and abstracts, 45 records were excluded, leaving 28 citations for further assessment. However, 8 of these citations were also eliminated due to incomplete data and contents. Ultimately, 20 articles (February 2020 to October 2023) were deemed eligible for the final analysis (10, 12-30) (Table 1). The final assessment of study quality, the applicability of primary diagnostic accuracy studies, and the risk of bias were assessed based on the QUADAS-2 tool. It assesses study quality and bias risk by looking at patient selection, index test, reference standard, and flow/timing. Four phases have been defined in the application of QUADAS-2, including (1) summarizing the questions reviewed; (2) tailoring the tool to the review and producing review-specific guidance; (3) constructing a flow diagram for the primary study; and (4) assessing the risk of bias and concerns regarding applicability. All 16 studies had a low risk of bias and were of good quality, making the pooled results persuasive (Figure 2). To reach the final judgment on the results, the comprehensive meta-analysis (CMA) software version 3.0 (Biostat, Englewood, NJ 07631 USA) was employed.

4. Results

To evaluate the frequency of MIS-C-related cardiac abnormalities using selected keywords, 20 studies were analyzed (including 28 patients, 18 men, and 9 women consisting of individuals aged between 23 and 96 years, with an average age of 62 years). Publications from February 2020 to October 2023 were evaluated, with contributions from multiple countries (Table 1). Among the 20 published studies, 19 were presented as case reports, and one was presented as a case series. Reports of myocardial infarction following vaccination almost included both Eastern and Western countries, and it was independent of the type of society. However, the occurrence of acute myocardial infarction was mostly

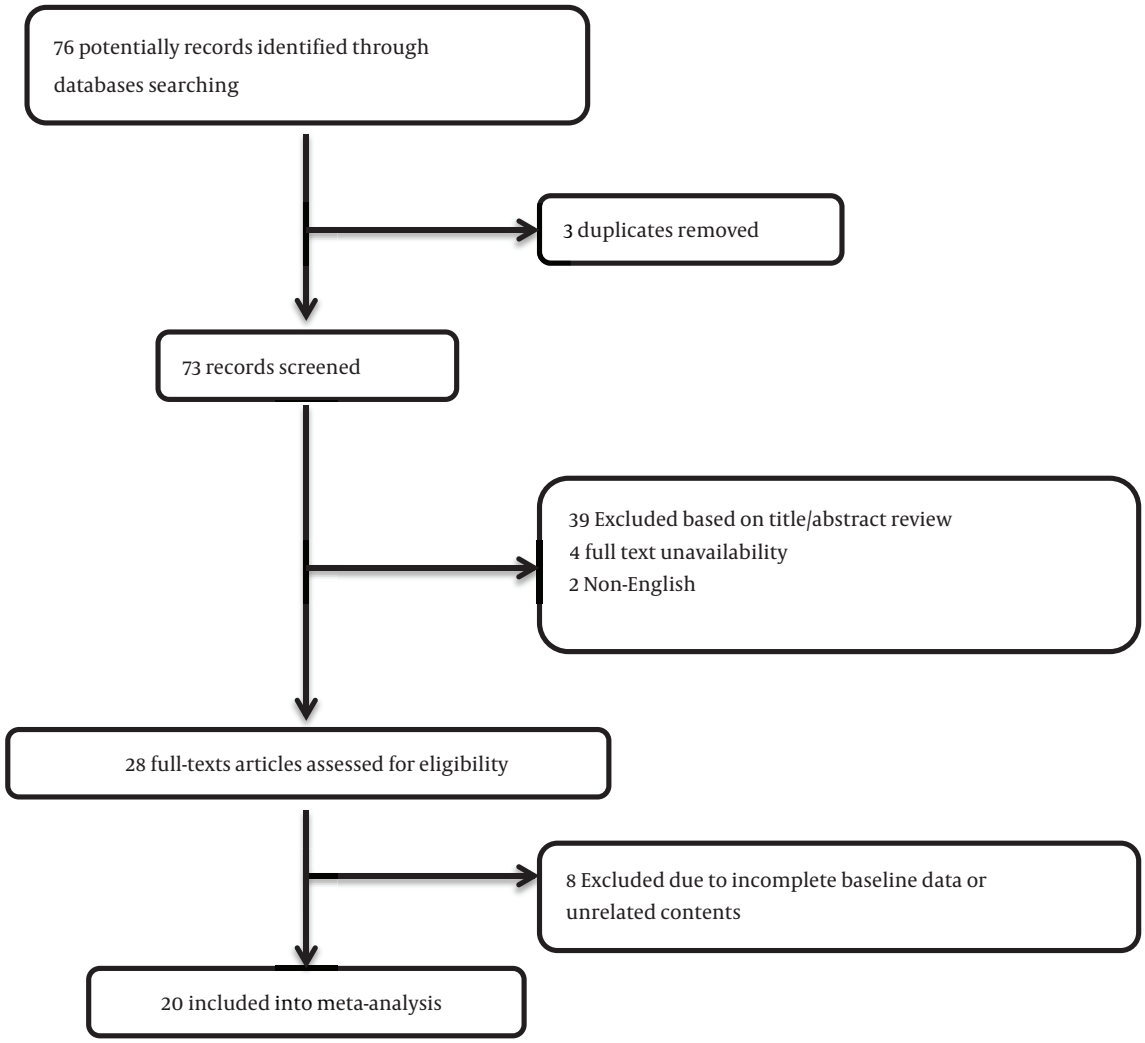

Figure 1. The flowchart of screening the eligible studies

related to SARS-CoV-2-based messenger RNA (mRNA) and viral vector vaccines. In this regard, of 28 vaccinated patients who suffered post-vaccination myocardial infarction, this cardiac event occurred following vaccination by AstraZeneca vaccine in 9 patients, and 10 events occurred following vaccination by Pfizer-BioNTech COVID-19 Vaccine, and 3 cases by Moderna, 2 cases by coronaVac, 2 cases by Covishield, 1 case by Sinovac, and 1 case by Sionopham. Regarding the time of occurrence of myocardial infarction, this cardiac attack occurred after the first vaccination in 24 out of 28 patients affected and after the second time in other patients (myocardial infarction after AstraZeneca was inclusively after the first dose, but myocardial infarction following other vaccines was after the first or second dose. The time of occurrence of myocardial infarction was also very different between different types of vaccines and varied between 15 minutes and 21 days after vaccination (average 2.8 days after vaccination). Most of the myocardial infarctions that occurred after vaccination were of the ST-segment elevation type (STEMI), which indicated the extent and severity of myocardial involvement following the inoculation of vaccines. More than two-thirds of myocardial infarction cases occurred in patients who had significant clinical history, including hypertension (32%), diabetes mellitus (28%), hyperlipidemia (25 %), history of renal failure (11%), history of coronary heart disease (7%), and history of smoking (7%). Concerning

	Patient selection	Index test	Outcomes	Flow and timing
Badaró, 2023	+	+	+	+
Baronti, 2022	+	+	?	+
Barsha, 2021	+	+		+
Boivin, 2021	+	?		+
Boudihi, 2022	+	+	?	+
Chatterjee, 2021	+	+	?	+
Chiang, 2021	+	+	+	+
Flower, 2021	+	?	+	+
Hsu, 2022	+	+	+	+
Huang, 2022	+	+	+	+
Huang, 2021	+	?	+	+
Iqbal, 2022	+	+	+	+
Kawamura, 2022	?	+	+	+
Kurozumi, 2022	+	+	+	+
Lee, 2022	+	?	+	+
Maadarani, 2021	+	+	+	+
Mishra, 2022	?	+	+	+
Özdemir, 2021	+	+	+	+
Panthong, 2021	+	?	+	+
Sung, 2021	+	+	+	+

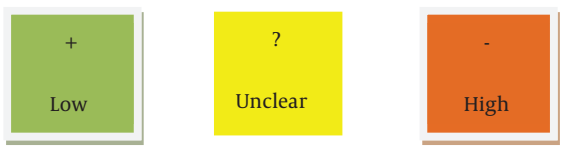

Figure 2. Assessment of the risk of bias

Table 1. The Details of the Studies Evaluated

Authors	Year	Country	Study Type	Type of Vaccine	Vaccine Time	Time of Myocardial Infarction Occurrence After Vaccination	Type of Myocardial Infarction	Gender	Age	Medical History	Outcome
Badaro et al. (10)	2023	Brazil	Case report	Pfizer	First	8 hours	STEMI	Male	23	WPW	Survived
Baronti et al. (12)	2022	Italy	Case series	Pfizer	First	48 hours	STEMI	Male	69	DM, COPD	Died
						8 hours	STEMI	Male	58	-	Died
						21 days	STEMI	Male	76	-	Died
						72 hours	STEMI	Male	68	HTN	Died
						24 hours	STEMI	Female	50	Smoking	Died
Barsha et al. (13)	2021	Bangladesh	Case report	Moderna	First	48 hours	NSTEMI	Male	77	DM, COPD	Survived
Boivin and Martin (14)	2021	USA	Case report	Moderna	First	1 hour	STEMI	Female	96	HTN	Survived
Boudihi et al. (15)	2023	Morocco	Case report	Sinopharm	Second	24 hours	STEMI	Male	23	-	Survived
Chatterjee et al. (16)	2021	India	Case report	Covishield	First	48 hours	STEMI	Male	63	-	Survived
Chiang et al. (17)	2021	Taiwan	Case report	AstraZeneca	First	8 days	STEMI	Female	75	RF	Survived
Flower et al. (18)	2021	UK	Case report	AstraZeneca	First	8 days	STEMI	Male	40	-	Survived
Hsu et al. (19)	2022	Taiwan	Case report	AstraZeneca	First	9 days	STEMI	Male	33	Obesity, HLP	Died
Huang et al. (20)	2022	Taiwan	Case report	AstraZeneca	First	72 hours	STEMI	Female	78	DM, RF	Survived
				AstraZeneca	First	72 hours	NSTEMI	Male	89	DM, HTN	Survived
				AstraZeneca	First	5 days	STEMI	Female	87	Colon cancer	Survived
Huang et al. (21)	2022	Taiwan	Case report	AstraZeneca	First	2 hours	STEMI	Male	60	-	Survived
Iqbal et al. (22)	2022	Pakistan	Case report	Moderna	First	3 hours	NSTEMI	Male	61	DM, HTN, IHD	Survived
Kawamura et al. (23)	2023	Japan	Case report	Pfizer	Second	19 hours	STEMI	Female	76	HTN, HLP, asthma	Survived
Kurozumi et al. (24)	2022	Japan	Case report	Pfizer	Second	15 min	STEMI	Female	70	DM, HTN, HLP	Survived
Lee et al. (25)	2022	Taiwan	Case report	AstraZeneca	First	7 days	STEMI	Male	85	RF	Survived
Maadarani et al. (26)	2021	Kuwait	Case report	AstraZeneca	First	1.5 hours	STEMI	Female	62	DM, HTN, HLP	Survived
Mishra et al. (27)	2022	India	Case report	Covishield	First	12 hours	STEMI	Male	68	HTN	Survived
Ozdemir et al. (28)	2021	Turkey	Case report	Sinovac	First	15 min	STEMI	Female	41	-	Survived
Panthong et al. (29)	2022	Thailand	Case report	CoronaVac	Second	18 hours	STEMI	Male	48	DM, HTN, HLP	Survived
				CoronaVac	First	12 hours	NSTEMI	Male	50	IHD	Survived
Sung et al. (31)	2021	USA	Case report	Pfizer	First	24 hours	STEMI	Female	68	HTN, HLP, smoking	Survived
				Pfizer	First	24 hours	NSTEMI	Male	42	HLP	Survived

Abbreviations: HLP, hyperlipidemia; HTN, hypertension; DM, diabetes mellitus; IHD, ischemic heart disease; RF, renal failure; STEMI, ST-segment elevation type.

survival outcomes following post-vaccination myocardial infarction, 22 out of 28 patients survived and were discharged from the hospital in good condition; however, 6 cases died within hospitalization.

5. Discussion

Twenty studies were analyzed with 28 patients who experienced myocardial infarction after receiving COVID-19 vaccines. Reports occurred in various countries, with most cases following mRNA and viral vector vaccines. Myocardial infarction occurs after the first vaccination in most cases, with a time frame of 15 minutes to 21 days after vaccination. Most affected patients had significant clinical history, but 22 survived, and 6 died during hospitalization. Most of the deaths due to COVID-19 are reported due to extensive pulmonary involvement and decreased arterial oxygen saturation, followed by

cardiac complications, especially ischemic heart attacks and cardiomyopathy (32-34). It is interesting to note that these deaths occurred not only after contracting COVID-19 but, in some cases, after vaccination against the disease, and most of these deaths occurred shortly after the vaccination and in the form of acute ischemic heart attacks. Information about the causes of myocardial infarction after vaccination against COVID-19 is limited and remains at the level of hypothesis. Vaccination can cause a prothrombotic condition similar to autoimmune heparin-induced thrombocytopenia (35). In other words, stress caused by the vaccination against COVID-19 can result in demand ischemia, resulting in cardiac events (36). Myocardial infarction after vaccination can be caused by Kounis syndrome, which is an allergic reaction that triggers vasospasm (37). According to our finding that most patients had a positive clinical history in terms of cardiovascular risk factors, the existence of the same underlying risk factors can be considered as a risk profile for the occurrence of acute myocardial infarction after vaccination. The existence of the same underlying risk factors can be considered as a risk profile for the occurrence of acute myocardial infarction after vaccination. But whether the viral vector or RNA virus used in the vaccine can be a trigger for inflammatory reactions and damage to the myocardium is still a hypothesis. This hypothesis becomes stronger when most of the cardiovascular attacks occurred after vaccination related to vaccines based on virus vectors or virus genomes. Moreover, vaccine-related thromboembolic events have been observed with such vaccines (38, 39), and it is strongly hypothesized that the thrombotic reaction following vaccination, especially following vaccines based on the virus genome, can be a trigger for ischemic heart attacks. As recently described, thrombosis and thrombocytopenia occurred 6 to 24 days after the first dose of the COVID-19 vaccination (40). In general, although the occurrence of acute myocardial infarction has been an uncommon phenomenon following vaccination against COVID-19 (31) (prevalence less than three-thousandths of a percent), to achieve high safety of these types of vaccines, biotechnological modification of the relevant vaccines is still necessary.

5.1. Suggestions

In the future, the relationship between the 1st, second, and third doses of vaccines and myocardial infarction could be evaluated in a wide range and much more research.

Footnotes

Authors' Contribution: Nima Rahimi Petrudi conceived and designed the evaluation and drafted the manuscript, participated in designing the evaluation, performed parts of the statistical analysis, and helped to draft the manuscript. Mostafa Abdollahi re-evaluated the clinical data, revised the manuscript, performed the statistical analysis, revised the manuscript, and collected and interpreted the clinical data. Iraj Mirzaii-Dizgah re-analyzed the clinical and statistical data and revised the manuscript. All authors read and approved the final manuscript.

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