Cardiovascular Topics

Association between Pfizer-BioNTech mRNA vaccine and myocardial infarction: clinical and angiographic insights

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Abstract

Objective: With the widespread administration of the BioNTech mRNA-based COVID-19 vaccine, there is a need to evaluate its potential effects on cardiovascular health, particularly its association with myocardial infarction (MI). This study aimed to investigate the relationship between BioNTech vaccination and MI, as well as its impact on clinical and angiographic parameters.

Methods: A retrospective analysis was conducted at the Eskisehir Osmangazi University, Eskisehir City Hospital, between April 2020 and May 2023 on a cohort of 1 151 patients hospitalised with MI. The patients were stratified into a BioNTech+ (vaccinated) and a BioNTech– (unvaccinated) groups. Medical records were reviewed for demographic information, clinical data and angiographic findings. Statistical analyses were performed, including logistic regression models adjusting for potential confounders.

Results: The BioNTech– group had a higher mean number of percutaneous transluminal coronary angioplasty procedures and stents compared to the BioNTech+ group. Haematological parameters and lipid profiles showed some discrepancies between the two groups. The BioNTech– group had higher white blood cell and platelet counts, while also exhibiting a higher mean low-density lipoprotein cholesterol level. The prevalence of co-morbidities and cardiovascular risk factors differed between the groups.

Conclusion: This study found associations between the BioNTech vaccination and clinical and angiographic parameters in patients with MI.

Keywords: angiographic parameters, BioNTech vaccine, cardiovascular health, COVID-19, myocardial infarction, vaccination

Submitted 7/11/23; accepted 22/11/23

Cardiovasc J Afr 2023; online publication www.cvja.co.za

DOI: 10.5830/CVJA-2023-062

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With the emergence of COVID-19, vaccination efforts have been a key strategy to mitigate the impact of the pandemic. BioNTech, an mRNA-based COVID-19 vaccine, has been widely administered.[1] While the vaccine has demonstrated efficacy in preventing COVID-19, there is a need to evaluate its potential effects on cardiovascular health, particularly its association with myocardial infarction (MI).

There is limited evidence to suggest a direct association between mRNA vaccines and MI. There have been some studies suggesting an association between vaccines and MI.[2-5] However, it should be noted that most of these studies are often based on case reports and are related to early reactions following vaccination, occurring within a short period (24 hours) after vaccination. They have not provided answers to questions regarding the long-term effects of vaccines and whether they pose an increased risk for MI in the chronic process, their potential to cause MI in young individuals, or their influence on factors such as lesion severity and the extent of diseased vessels. This study was conducted with the aim of seeking answers to these questions.

By investigating the relationship between BioNTech vaccination and MI, as well as its impact on clinical and angiographic parameters, this study aimed to contribute to the growing body of knowledge on the potential cardiovascular effects of COVID-19 vaccines. The findings have implications for patient care, risk stratification and public health strategies.

Methods

An analysis was conducted on a cohort of 1 151 patients hospitalised with a diagnosis of MI. The patients were recruited from two tertiary hospitals and were stratified into two groups based on their vaccination status: individuals who received the BioNTech vaccine (BioNTech+, n = 490), and those who did not receive the vaccine (BioNTech–, n = 661). Patients who were hospitalised with a diagnosis of MI between April 2020 and May 2023 were screened and patients who met the inclusion criteria were consecutively included in the study.

Medical records, including demographic information, clinical data and angiographic findings were reviewed for each patient. Patients who were hospitalised due to MI, older than 18 years and had coronary angiography were included in the study. Patients whose vaccination status and whether they were diagnosed with COVID-19 were unknown, and patients whose laboratory and angiography information could not be accessed were excluded from the study.

The primary outcome was the association between BioNTech vaccination and the occurrence of MI. Secondary outcomes included the extent and characteristics of vessels involved in MI, the prevalence of different types of MI (ST-segment elevation MI, non-ST-segment elevation MI), and the age at onset of MI.

Ethical approval for this study was obtained from local ethics committee (decision date: 15/03/2023, decision no: ESH/GOEK 2023/1), ensuring patient confidentiality and adherence to ethical guidelines.

Statistical analyses

Statistical analyses were performed using appropriate methods. Continuous variables are expressed as means ± standard deviations or medians with interquartile ranges, while categorical variables are presented as frequencies and percentages. Group comparisons were conducted using the independent *t*-test, Mann–Whitney *U*-test or chi-squared test, as appropriate. Multivariate logistic regression models were utilised to determine the independent association between BioNTech vaccination and the risk of MI, adjusting for potential confounders.

Results

Table 1 reveals that there was no significant difference in age between the BioNTech– and BioNTech+ groups ($p = 0.520$), indicating that age was comparable among the vaccinated individuals. However, significant differences were observed in several other variables. The BioNTech– group exhibited a higher mean percutaneous transluminal coronary angioplasty (PTCA) number compared to the BioNTech+ group ($p < 0.001$). Similarly, the BioNTech– group had a higher mean stent number compared to the BioNTech+ group ($p < 0.001$). These findings suggest that individuals who received the BioNTech– vaccine may have undergone more invasive procedures for coronary artery disease (CAD) treatment compared to those who received the BioNTech+ vaccine.

The BioNTech– group exhibited a higher mean white blood cell count (WBC) compared to the BioNTech+ group ($p = 0.030$), suggesting a potential difference in immune response. Moreover, the BioNTech– group had a higher mean platelet count (PLT) compared to the BioNTech+ group ($p < 0.001$), indicating a possible variation in thrombotic risk.

Table 1. Descriptive statistics and group comparisons

Variables	*BioNTech–*	*BioNTech+*	t/*f* (*df*)	p-*value*
Age	58.84 ± 16.930	58.41 ± 11.232	0.64 (432)	> 0.05
PTCA number	1.66 ± 0.806	0.88 ± 0.458	9.18 (432)	0.000
Stent number	1.10 ± 0.677	0.87 ± 0.483	5.15 (432)	0.000
Hg	14.50 ± 2.088	14.49 ± 4.232	0.02 (432)	> 0.05
WBC	11.54 ± 7.542	10.71 ± 3.405	2.17 (432)	> 0.05
PLT	254.31 ± 76.510	234.39 ± 61.170	4.02 (432)	0.000
HDL-C	41.41 ± 11.933	40.19 ± 9.657	1.80 (432)	> 0.05
LDL-C	120.57 ± 37.567	115.00 ± 34.807	2.58 (432)	> 0.05
Total cholesterol	188.01 ± 45.711	187.04 ± 37.751	0.45 (432)	> 0.05
Triglycerides	147.29 ± 111.932	159.44 ± 93.084	–1.86 (432)	> 0.05

PTCA: percutaneous transluminal coronary angioplasty; Hg: haemoglobin; WBC: white blood cell count; PLT: platelets; HDL-C: high-density lipoprotein cholesterol; LD-CL: low-density lipoprotein cholesterol; *t*/f (df): *t*-value divided by degrees of freedom; *p*-value < 0.05 is considered statistically significant.

Lipid profile analysis revealed that the BioNTech– group had a higher mean low-density lipoprotein cholesterol (LDL-C) level compared to the BioNTech+ group ($p = 0.010$). Additionally, the BioNTech+ group exhibited a slightly higher mean triglyceride level compared to the BioNTech– group, although the difference did not reach statistical significance ($t = –1.86$, df = 432, $p = 0.064$).

Table 2 presents the group comparisons for categorical variables. The BioNTech– group had a higher proportion of individuals with hypertension ($p < 0.001$), diabetes mellitus (DM) ($p < 0.001$) and CAD ($p < 0.001$) compared to the BioNTech+ group. Furthermore, a significantly higher proportion of individuals in the BioNTech+ group reported a history of congestive heart failure ($p = 0.000$).

Finally, Table 3 presents the results of logistic regression analysis to identify predictors of the outcome. Age did not have a significant effect on the outcome [B = 0.000, $p = 0.971$, Exp(B) = 1.000]. However, the involvement of one vessel [B = 1.223, $p = 0.004$, Exp(B) = 3.396] and two vessels [B = 1.058, $p = 0.011$, Exp(B) = 2.881] showed significant positive associations with the outcome, indicating that a higher number of affected vessels increased the odds of the outcome with the involvement of three vessels, while not statistically significant [B = 0.645, $p = 0.113$, Exp(B) = 1.906], the observed trend suggests a potential association.

Table 2. Group comparisons for categorical variables

Variables	*BioNTech–* n *(%)*	*BioNTech+* n *(%)*	p-*value*
Gender			> 0.05
Male	509 (77.0)	374 (76.3)	
Female	152 (23.0)	116 (23.7)	
HT	403 (61.1)	185 (37.8)	0.000
DM	285 (43.2)	77 (15.7)	0.000
Smoking	341 (51.7)	185 (37.8)	> 0.05
CAD	128 (18.4)	181 (36.9)	0.000
CHF	113 (38.9)	26 (62.2)	0.000
MI type			0.000
Anterior	116 (17.5)	89 (18.2)	
Inferior	204 (30.9)	85 (17.3)	
Lateral	9 (1.4)	1 (0.2)	
Posterior	3 (0.5)	0	
NSTEMI	329 (49.8)	315 (64.3)	
COVID	223 (33.7)	146 (29.8)	> 0.05
One vessel	350 (53.0)	296 (60.4)	0.000
Two vessels	177 (26.8)	125 (25.5)	0.012
Three or more vessels	120 (18.2)	61 (12.4)	> 0.05

HT: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; CHF: congestive heart failure; MI: myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; COVID: COVID-19; *p*-value < 0.05 is considered statistically significant.

Table 3. Predictors of outcome in logistic regression

Predictors	*B*	*p-value*	*Exp(B)*	*Interpretation*
Age	0.000	0.971	1.000	No significant effect on the outcome
One vessel	1.223	0.004	3.396	Higher: one vessel increases the odds of the outcome 3.4 times
Two vessels	1.058	0.011	2.881	Higher: two vessels increase the odds of the outcome 2.9 times
Three vessels	0.645	0.113	1.906	No significant effect on the outcome

Discussion

This study found associations between BioNTech mRNA vaccination and clinical and angiographic parameters in patients with MI, suggesting potential differences in disease severity and risk factors between the vaccinated and unvaccinated groups.

Firstly, it is important to highlight that age did not significantly differ between the BioNTech– and BioNTech+ groups, indicating that age distribution was comparable among vaccinated and unvaccinated individuals. This finding suggests that age may not be a confounding factor when evaluating the relationship between the BioNTech vaccine and MI.

In the study conducted by Aye *et al*., which examined 35 cases of MI following COVID-19, the average age was 55 years, and most of the cases were male.[4] This study also found a similar average age to that in our study, supporting the absence of evidence suggesting that the vaccine causes MI at an early age. In contrast to this, our study demonstrated no increase in MI cases associated with vaccination in the long term, specifically regarding gender-related cases.

The association between mRNA vaccines and MI is controversial. While some studies contend that these vaccines are linked to MI, others contend that the opposite is true. Some studies note that rare and serious adverse events have been reported following administration of mRNA vaccines, including myocarditis and acute MI.[6,7] However, Chui *et al.* discovered no increased risk of acute MI, stroke or pulmonary embolism after both doses of the BNT162b2 mRNA vaccine in individuals aged 75 years and up.[8]

The present investigation looked into the vaccine's relationship with MI character and features. Regarding clinical parameters, individuals in the BioNTech– group exhibited a higher mean number of PTCA procedures and stents compared to the BioNTech+ group. These results suggest that patients who did not receive the BioNTech vaccine may have had a higher burden of CAD, necessitating more invasive interventions for disease management.

Although it has been determined in many studies that vaccines are associated with many cardiovascular diseases, especially myocarditis and pericarditis, it has also been discussed whether this is the effect of the vaccine or the effect of the COVID-19 disease itself.[9-11] In one study, Botton *et al*. found that the Pfizer-BioNTech and Moderna-mRNA vaccines were not associated with an increased risk of cardiovascular events in adults under the age of 75 years. However, recipients of the Oxford-AstraZeneca vaccine had a greater risk of MI and pulmonary embolism in the second week after vaccination. The study suggests that adenoviral-based vaccines may be associated with an increased incidence of MI and pulmonary embolism in individuals aged 18 to 74 years.[12]

This suspicion has been dispelled, as our study found no difference in COVID-19 disease prevalence between the two groups. These findings should be interpreted cautiously, as they do not establish a causal relationship between the vaccine and the need for invasive procedures.

This information can be interpreted in two ways. Firstly, the vaccine itself may have an impact on the thrombosis mechanism, leading to the formation of acute rather than chronic non-lethal lesions that result in a shorter time frame for acute thrombosis. However, this direct relationship could not be established with this study.

Previous studies have shown an association between the vaccine and early-stage MI,[4] but long-term outcomes have not been investigated. As we will discuss in more detail below, the unvaccinated group had a higher risk profile and a higher likelihood of developing more resistant lesions during the chronic process, while the vaccinated group, despite having fewer risk factors, still experienced MI cases.

Secondly, as mentioned above, the vaccine may reduce the likelihood of patients with risk factors for CAD experiencing MI.[10] Although the vaccinated group had fewer risk factors, there were still cases of MI, while the unvaccinated group had a higher probability of developing more resistant lesions in the chronic process.

A frequently debated topic in the literature regarding vaccines is the issue of thrombosis and immune response. Thrombosis was the most frequently reported event, followed by stroke, myocarditis, MI, pulmonary embolism and arrhythmia. Thrombosis was more common with the BNT162b2 vaccine, while stroke was more common with mRNA-1273 vaccine.[13]

Haematological parameters also demonstrated some discrepancies between the two groups. The BioNTech– group had a higher mean WBC and PLT compared to the BioNTech+ group. These findings suggest the possibility of differing immune responses and thrombotic risk profiles between vaccinated and unvaccinated individuals. The elevated WBC count suggests a potential difference in immune response between the two groups.

It is worth noting that previous studies have reported an association between inflammation, immune response and the risk of cardiovascular events, including MI.[14] The observation of lower WBC and PLT counts in the vaccinated group compared to the control group in the long term may actually steer us away from establishing a direct relationship between the vaccine and MI.

In terms of lipid profile, the study found a higher mean LDL-C level in the BioNTech– group compared to the BioNTech+ group. While the difference was statistically significant, it is important to note that the clinical significance of this finding in relation to MI risk remains uncertain. Elevated LDL-C levels are well-established risk factors for the development of atherosclerosis and cardiovascular disease.[15] However, further research is required to determine the clinical implications of the observed difference in LDL-C levels between the two groups and its potential contribution to the risk of MI.

When examining the risk factors for CAD, it was observed that hypertension and DM were more prevalent in the unvaccinated group, while a history of CAD was more prevalent in the vaccinated group. Age, smoking and gender were found to be similar between the two groups. Therefore, it is difficult to state a definitive difference in risk factors between the two groups. However, it can be accepted that factors such as hyperlipidaemia, hypertension and DM, which are cardinal risk factors for CAD,[16] were more prevalent in the unvaccinated group, and the indirect interpretations we made regarding stent and PTCA numbers are also applicable here.

One of the other aspects we were curious about in this study was whether the vaccine had any effect on the frequency of ST-elevation myocardial infarction (STEMI). Significantly, a higher incidence of non-ST-elevation myocardial infarction (NSTEMI) was observed in the vaccinated group. We believe this is a subject that requires further investigation because NSTEMI

patients tend to have more co-morbidities compared to STEMI patients.[17] However, despite the relatively lower co-morbidity rate in the vaccinated group, a proportionally higher number of NSTEMI cases were observed. This can be interpreted in several ways.

Firstly, few studies mention a decrease in hospital admissions for MI during the pandemic.[18,19] Since the BioNTech vaccine was administered in our study country at a later stage, it is possible that the uncertainty surrounding the pandemic and the public belief in the need to stay at home resulted in a relatively more pronounced presentation of STEMI cases seeking hospital admission at the beginning of the pandemic. Although we strongly believe that this difference may be attributed to variations in patients' habits of seeking medical attention during the pandemic or temporary difficulties in accessing hospitals at the beginning of the pandemic period, it cannot be dismissed based on these data that the vaccine may have contributed to a greater increase in NSTEMI rates.

The occurrence of acute MI following vaccination has raised concerns regarding potential underlying mechanisms. One hypothesis suggests that vaccination triggers an autoimmune response targeting PLT, akin to the clinical manifestation observed in autoimmune heparin-induced thrombocytopaenia.[20,21] However, the presence of long-term post-vaccine effects on MI development remains uncertain.

However, it should be noted that while single-vessel involvement was significantly higher in the vaccinated group, and two-vessel involvement was significantly higher in the non-vaccinated group, there was no significant difference in terms of multi-vessel involvement between the two groups. Therefore, when analysed in a general context, based on these findings, it cannot be concluded that the vaccine increased the prevalence of MI with the involvement of multiple vessels. These data can give us information about two things. The vaccine has no long-term effect on the development of MI, and even if it has an effect, the development of MI proceeds by a mechanism similar to that of the unvaccinated.

It is crucial to contextualise these findings within the limitations of the study. The retrospective design and relatively small sample size may have introduced selection bias and limited the generalisability of the results. Additionally, the observational nature of the study precludes establishing a causal relationship between the BioNTech vaccine and MI. Confounding variables, including unmeasured co-morbidities or medication use, may have influenced the observed associations. Moreover, the study did not consider the timing of vaccination in relation to the occurrence of MI, which could potentially have impacted on the interpretation of the results.

Conclusion

This study provides insights into the potential relationship between the BioNTech mRNA-based COVID-19 vaccine and MI, along with its effects on various clinical and angiographic parameters. The findings suggest that patients who did not receive the BioNTech vaccine may have had a higher burden of CAD and associated co-morbidities. Variations in haematological parameters and lipid profiles between the BioNTech– and BioNTech+ groups further highlight potential differences in immune response, thrombotic risk and lipid metabolism.

References

1. Khurana A, Allawadhi P, Khurana I, Allwadhi S, Weiskirchen R, Banothu AK, *et al*. Role of nanotechnology behind the success of mRNA vaccines for COVID-19. *Nano Today* 2021; **38**: 101142.
2. Lopez Bernal J, Andrews N, Gower C, Gallagher E, Simmons R, Thelwall S, *et al*. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. *N Engl J Med* 2021; **385**(7): 585–594.
3. Boehmer TK, Kompaniyets L, Lavery AM, Hsu J, Ko JY, Yusuf H, *et al*. Association between COVID-19 and myocarditis using hospital-based administrative data – United States, March 2020 – January 2021. *MMWR Morb Mortal Wkly Rep* 2021; **70**(35): 1228–1232.
4. Aye YN, Mai AS, Zhang A, Lim OZH, Lin N, Ng CH, *et al*. Acute myocardial infarction and myocarditis following COVID-19 vaccination. *Q J Med* 2023; **116**(4): 279–283.
5. Kawamura Y, Yoshimachi F, Nanao T, Kasai S, Ikari Y. A case of ST-segment elevation myocardial infarction within 24 h of a third dose of COVID-19 mRNA vaccine. *Cardiovasc Revasc Med* 2022; **53S**: S313–316.
6. Anderson EJ, Rouphael NG, Widge AT, Jackson LA, Roberts PC, Makhene M, *et al.* Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. *N Engl J Med* 2020; **383**(25): 2427–2438.
7. Vidian V, Dikson N, Litanto V, Christy S, Jo J, *et al.* Emergence of the Sars-cov-2 Omicron variant: current treatments and vaccines For Covid-19. *Explor Res Hypothesis Med* 2023; 8(2): 157–170.
8. Wan EYF, Chui CSL, Lai FTT, Chan EWY, Li X, Yan VKC, *et al*. Bell's palsy following vaccination with mRNA (BNT162b2) and inactivated (CoronaVac) SARS-CoV-2 vaccines: a case series and nested case–control study. *Lancet Infect Dis* 2022; **22**(1): 64–72.
9. Klein NP, Lewis N, Goddard K, Fireman B, Zerbo O, Hanson KE, *et al*. Surveillance for adverse events after COVID-19 mRNA vaccination. *J Am Med Assoc* 2021; **326**(14): 1390–1399.
10. Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, *et al.* Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting. *N Engl J Med* 2021; **385**(12): 1078–1090.
11. Wong HL, Hu M, Zhou CK, Lloyd PC, Amend KL, *et al*. Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases. *Lancet* 2022; **399**(10342): 2191–2199.
12. Botton J, Jabagi MJ, Bertrand M, Baricault B, Drouin J, Le Vu S, *et al*. Risk for myocardial infarction, stroke, and pulmonary embolism following COVID-19 vaccines in adults younger than 75 years in France. *Ann Intern Med* 2022; **175**(9): 1250–1257.
13. Yasmin F, Najeeb H, Naeem U, Moeed A, Atif AR, Asghar MS, *et al*. Adverse events following COVID-19 mRNA vaccines: A systematic review of cardiovascular complication, thrombosis, and thrombocytopenia. *Immun Inflamm Dis* 2023; **11**(3): e807.
14. Libby P, Loscalzo J, Ridker PM, Farkouh ME, Hsue PY, Fuster V, *et al.* Inflammation, immunity, and infection in atherothrombosis: JACC review topic of the week. *J Am Coll Cardiol* 2018; **72**(17): 2071–2081.
15. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, *et al*. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019; **73**(24): e285–e350.
16. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, *et al*. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019; **140**(11): e596–e646. Erratum in: *Circulation* 2020; **141**(4): e60. Erratum in: *Circulation* 2020; **141**(16): e774.

17. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs A, Bhatt DL, *et al*. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2021; **42**(14): 1289–1367.
18. Pourasghari H, Tavolinejad H, Soleimanpour S, Abdi Z, Arabloo J, Bragazzi NL, *et al*. Hospitalization, major complications and mortality in acute myocardial infarction patients during the COVID-19 era: A systematic review and meta-analysis. *Int J Cardiol Heart Vasc* 2022; **41**: 101058.
19. Choi H, Lee JH, Park HK, Lee E, Kim MS, Kim HJ, *et al*. Impact of the COVID-19 pandemic on patient delay and clinical outcomes for patients with acute myocardial infarction. *J Korean Med Sci* 2022; **37**(21): e167.
20. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med* 2021; **384**(22): 2092–2101.
21. Wise J. Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. *Br Med J* 2021; **372**: 699.