

Acute Myocardial Infarction Within 24 Hours After COVID-19 Vaccination: Is Kounis Syndrome the Culprit?



In an important report published in the *American Journal of Cardiology*,¹ 2 patients (1 female and 1 male) who received the same COVID-19 vaccine messenger RNA-1273 (Moderna) developed acute myocardial infarction 1 day after the first dose. The authors speculated that the Moderna vaccine can induce an antibody response with a lipid-nanoparticle-encapsulated messenger RNA, whereas the ChAdOx1 nCoV-19 vaccine (AstraZeneca) can trigger an immune response by the nCoV-19 spike protein.

Recent reports have shown Kounis hypersensitivity-associated acute myocardial infarction to be associated with other COVID-19 vaccines including BNT162b2 (Pfizer-BioNTech),² Covishield vaccine,^{3,4} and Sinovac (Coronavac)⁵ in addition to Moderna^{2,6,7} and AstraZeneca.⁷

Kounis syndrome is a condition associated with hypersensitivity reactions caused by drugs, metals, environmental exposures, conditions, and foods.⁸ In a recent report that dealt with 2 patients who developed myocarditis after getting vaccinated with Moderna and Pfizer-BioNTech, respectively, endomyocardial biopsy specimens showed inflammatory infiltrates comprising eosinophils and other interacting inflammatory cells, including T cells, B cells, plasma cells, and macrophages, indicating hypersensitivity reactions.⁹ Indeed, all currently used vaccines contain excipients (constituents of a pharmaceutical form apart from the active substance) that are speculated to induce hypersensitivity reactions.

The viral vector Covishield vaccine, which is similar to AstraZeneca and manufactured in India, contains polysorbate 80, disodium edetate dihydrate (ethylenediaminetetraacetic acid), and aluminum hydroxide. The Moderna vaccine contains polyethylene glycol and tromethamine, also known as trometamol. The Pfizer-BioNTech vaccine contains polyethylene glycol. The Johnson & Johnson vaccine contains polysorbate 80. The Sputnik V vaccine contains polysorbate 80 and disodium ethylenediaminetetraacetic acid dehydrate. The Sinovac (Coronavac), which is manufactured in

China, contains disodium hydrogen phosphate, sodium dihydrogen phosphate monohydrate, and sodium chloride.

These excipients are also found in creams, ointments, lotions, other cosmetics, various dental materials, and anticancer drugs which could sensitize their users. It is estimated that 1% to 5.4% of the population is already sensitized to cosmetics or cosmetic ingredients.¹⁰ Free polysorbate oncology medications are already in the market.¹¹ Alternatives to these excipients, such as alkylsaccharides, are promising agents because they can reduce immunogenicity, improve stability, suppress oxidative damage problems, and may prevent thrombotic and cardiovascular events.¹² COVID-19 free allergenic vaccines would be beneficial.

Disclosures

The authors have no conflicts of interest to declare.

Nicholas G. Kounis, MD, PhD

Ioanna Koniari, MD, PhD

Virginia Mplani, MD, PhD

Sophia N. Kouni, MSc, PhD

Panagiotis Plotas, MD, PhD

Grigorios Tsigkas, MD, PhD

Department of Cardiology, University of Patras
School of Medicine, Patras, Greece

18 September 2021

1. Sung JG, Sobieszczyk PS, Bhatt DL. Acute myocardial infarction within 24 hours after COVID-19 vaccination. *Am J Cardiol* 2021;156:129–131.
2. Tajstra M, Jaroszewicz J, Gąsior M. Acute coronary tree thrombosis after vaccination for COVID-19. *JACC Cardiovasc Intv* 2021;14:e103–e104.
3. Chatterjee S, Ojha UK, Vardhan B, Tiwari A. Myocardial infarction after COVID-19 vaccination-casual or causal? *Diabetes Metab Syndr* 2021;15:1055–1056.
4. Srinivasan KN, Sathyamurthy I, Neelagandan M. Relation between COVID-19 vaccination and myocardial infarction—casual or coincidental? *IHJ Cardiovascular Case Rep* 2021;5:71–74.
5. Özdemir İH, Özlek B, Özen MB, Gündüz R, Bayturan Ö. Type 1 Kounis syndrome induced by inactivated SARS-COV-2 vaccine [published online May 7, 2021]. *J Emerg Med* doi:10.1016/j.jemermed.2021.04.018.
6. Boivin Z, Martin J. Untimely myocardial infarction or COVID-19 vaccine side effect. *Cureus* 2021;13:e13651.
7. Maadarani O, Bitar Z, Elzouairy M, Nader M, Abdelfatah M, Zaalouk T, Mohsen M, Elhabibi M. Myocardial infarction post COVID-19 vaccine - coincidence, Kounis syndrome or other

explanation - time will tell. *JRSM Open* 2021;12:20542704211025259.

8. Kounis NG, Koniari I, de Gregorio C. COVID-19 and Kounis syndrome: deciphering their relationship. *Balkan Med J* 2021;38:145–149.
9. Verma AK, Lavine KJ, Lin CY. Myocarditis after COVID-19 mRNA vaccination. *N Engl J Med* 2021;385:1332–1334.
10. Lyapina MG, Stoyanova Dencheva M. Contact sensitization to ingredients of dental materials and cosmetics in dental students: a pilot study. *Cent Eur J Public Health* 2019;27:73–77.
11. Schwartzberg LS, Navari RM. Safety of polysorbate 80 in the oncology setting. *Adv Ther* 2018;35:754–767.
12. Kounis NG, Koniari I, de Gregorio C, Assimakopoulos SF, Velissaris D, Hung MY, Mplani V, Saba L, Brinia A, Kouni SN, Gogos C, Giovannini M, Novembre E, Arumugham V, Ricke DO, Soufras GD, Nugent K, Sestili P, Malone RW. COVID-19 disease, women's predominant non-heparin vaccine-induced thrombotic thrombocytopenia and Kounis syndrome: a passepartout cytokine storm interplay. *Biomedicines* 2021;9:959.

<https://doi.org/10.1016/j.amjcard.2021.09.032>

Gender Differences in the Outcomes of Transcatheter Mitral Valve Implantation



Transcatheter mitral valve implantation has emerged as a less invasive treatment than conventional surgery for the treatment of severe mitral regurgitation in patients with prohibitive surgical risk.^{1,2} Previous studies have demonstrated significantly worse outcomes in women compared with men undergoing cardiac surgery, including coronary artery bypass graft,³ surgical aortic valve replacement,⁴ or mitral valve surgery.⁵ In contrast, results of the existing studies on transcatheter valvular heart disease interventions are favorable with improved outcomes in women undergoing transcatheter aortic valve implantation (TAVI)⁴ and have comparable outcomes in both genders in patients undergoing transcatheter mitral valve repair.^{6,7} However, the data on the impact of gender on the outcomes of patients undergoing transcatheter mitral valve implantation are limited. Therefore, we used a nationwide cohort to ascertain the gender differences in outcomes of patients undergoing transcatheter mitral valve implantation. We identified all the hospitalizations of patients aged ≥ 18 years who underwent