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Kounis syndrome in the era of COVID-19: pathophysiology, clinical challenges, and therapeutic approaches

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Abstract: Kounis syndrome, first described in 1991, refers to allergic or hypersensitive reactions that result in acute coronary syndrome (ACS). In addition to SARS-CoV-2, this disease has enhanced our comprehension of viral infections, inflammatory reactions, and cardiovascular repercussions. The COVID-19 pandemic has exposed the occurrence of cardiac damage, arrhythmias, and thrombotic events that are associated to the SARS-CoV-2 virus, thereby making the understanding of their development more complex. This research explores the complex correlation between Kounis syndrome and COVID-19, encompassing the phenomena of cytokine storms and endothelial dysfunction. Diagnosing Kounis syndrome in the context of COVID-19 presents challenges, nevertheless, it is imperative to distinguish it from other cardiovascular disorders. The identification of risk factors and predisposing situations that can exacerbate Kounis syndrome in COVID-19 patients is highlighted, with a particular focus on patient assessment. The care of Kounis syndrome in COVID-19 necessitates a multidisciplinary strategy that involves collaboration among cardiologists, allergists, and other specialists. Possible therapies encompass epinephrine, antihistamines, corticosteroids, cardiovascular interventions, as well as long-term surveillance and measures to reduce risk. Additional investigation should include epidemiological enquiries, experimental frameworks, and advancements in diagnostic and therapeutic approaches. Comprehending the connection between viral infections and coronary syndromes caused by allergies is crucial for clinical practice and the well-being of patients. This review explores the neurobiological similarities and clinical implications of Kounis syndrome and COVID-19, aiming to enhance comprehension and treatment of this intricate clinical scenario.

Keywords: Acute Coronary Syndrome; Allergic Reactions; COVID-19; Inflammatory Mediators; Kounis Syndrome

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1. Introduction

The term Kounis syndrome was initially coined in 1991 by Greek cardiologists Nicholas G. Kounis and George N. Gongadze to describe an interesting combination of allergic or hypersensitivity reactions that cause acute coronary syndrome (ACS) (1). The knowledge of the intricate pathophysiology and clinical implications of Kounis syndrome is evolving along with our comprehension of it, which stimulates further investigation into its subtleties. Additionally, the outbreak of SARS-CoV-2 and the COVID-19 pandemic has brought about a new level of understanding about the relationships that exist between viral infections, inflammatory responses, and cardiovascular repercussions (2,3).

Despite COVID-19 continues to be most commonly associated with respiratory symptoms, an increasing amount of research links the virus to a wide range of cardiovascular symptoms, such as myocardial damage, myocarditis, arrhythmias, and thrombotic events, highlighting the complex pathophysiology of the illness (3,4). In subsequent sections, we will delve into the pathophysiological underpinnings of both Kounis syndrome and COVID-19, exploring their potential mechanistic overlap and synergistic effects. We will elucidate the clinical manifestations and diagnostic challenges inherent in this dual pathology, highlighting the importance of a multidisciplinary approach to patient assessment and management (1,5). Furthermore, we will discuss predisposing factors and risk stratification strategies tailored to this unique clinical scenario, recognizing the need for individualized care in the face of varying patient presentations and disease severity (1,6,7). Finally, we will outline therapeutic approaches encompassing both pharmacological interventions and adjunctive measures aimed at mitigating the inflammatory cascade, optimizing coronary perfusion, and attenuating viral replication, with a focus on evidence-based recommendations and emerging treatment paradigms (1,8,9). Through this comprehensive analysis, we aim to contribute to the evolving discourse surrounding the interface between allergic-mediated coronary syndromes and viral infections, fostering a deeper understanding of their interplay and its implications for clinical practice.

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2. Pathophysiology of Kounis syndrome

Kounis syndrome, also known as allergic angina or allergic myocardial infarction, is a condition that involves the combination of allergic or hypersensitive reactions with acute coronary syndromes. This disease is a result of the release of systemic histamine, tryptase, leukotrienes, and cytokines following an allergic attack. Mast cells that have been activated, along with other immune cells that carry out a specific activity, produce substances that encourage the contraction of the coronary arteries, impair the function of the cells lining the arteries, and induce the rupture of plaque. These events can lead to a lack of blood supply to the heart muscle or a heart attack. Allergic mast cell degranulation results in the production of vasoactive chemicals that cause constriction, permeability, and contraction of the coronary arteries (1). The aforementioned actions have the potential to render plaques unstable, hence initiating the occurrence of rupture and thrombus in pre-existing atherosclerosis (8). Acute coronary syndrome is caused by a decrease or complete stoppage of blood flow in the coronary arteries. Pro-inflammatory substances boost the process of platelet clumping and the tendency of coronary blood vessels to form blood clots, hence elevating the risk of a heart attack (18). In type I, the primary mechanism is coronary spasm in people who have normal coronary arteries and no risk factors for coronary artery disease. In type II, the allergic reaction leads to the erosion or rupture of plaque. Stent thrombosis develops in type III. In order to diagnose and treat patients, it is necessary to have a comprehensive understanding of allergies and cardiovascular mechanisms, as well as the connection between immunological activation and coronary artery pathology (Figure1).

3. COVID-19 and cardiovascular complications

The SARS-CoV-2 virus, responsible for the COVID-19 pandemic, primarily targets the respiratory system but can also have significant cardiovascular implications (2,3). Multiple mechanisms have been proposed to explain the diverse cardiovascular complications associated with COVID-19 infection (10-12). Firstly, SARS-CoV-2 can directly infect and damage various cell types, including endothelial cells lining blood vessels and cardiomyocytes in the heart muscle, through binding to the angiotensin-converting enzyme 2 (ACE2) receptor present in these cells (3).

This direct viral injury can lead to endothelial dysfunction, compromising blood vessel function, as well as myocardial inflammation, potentially contributing to myocardial injury or arrhythmias. Secondly, COVID-19 is characterized by a dysregulated immune response and a cytokine storm, with elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-), and C-reactive protein (CRP) (2). This systemic inflammation can further exacerbate endothelial dysfunction, promote thrombosis (blood clotting), and cause myocardial injury, increasing the risk of cardiovascular complications. Thirdly, COVID-19 has been linked to an increased risk of thromboembolic events, including life-threatening conditions like pulmonary embolism, deep vein thrombosis, and acute coronary syndromes (3). The underlying mechanisms may involve endothelial injury, inflammation-induced hypercoagulability (increased clotting tendency), and stasis (impaired blood flow) due to immobility or critical illness (11).

4. Kounis syndrome and COVID-19: potential pathophysiological interactions

The COVID-19 pandemic has illuminated the intricate pathophysiological interplay between viral infections, dysregulated inflammatory responses, and cardiovascular complications (12). Although Kounis syndrome, defined as an acute coronary syndrome precipitated by inflammatory stimuli, is a relatively uncommon clinical entity, the potential interactions between COVID-19 and Kounis syndrome warrant meticulous investigation and elucidation (6). A key potential mechanism involves the cytokine storm and aberrantly elevated levels of inflammatory m ediators, s uch as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-), and C-reactive protein (CRP), observed in COVID-19 patients (2). These inflammatory mediators have been implicated in the pathogenesis of Kounis syndrome, as they can induce coronary vasospasm, plaque destabilization, and thrombus formation (2). Moreover, both COVID-19 and Kounis syndrome share associations with endothelial dysfunction and an augmented propensity for thrombotic events (3,11). The endothelial injury and pro-coagulant state prevalent in COVID-19 patients may potentiate the development of Kounis syndrome by exacerbating coronary vasospasm, plaque rupture, and thrombus formation (3). Notably, COVID-19 has been implicated in various hypersensitivity reactions, including cutaneous manifestations, urticaria, and anaphylaxis, which can potentially act as precipitating triggers for Kounis syndrome by eliciting the release of inflammatory mediators and induce coronary vasospasm or plaque destabilization (6). Furthermore, the direct viral injury and myocardial inflammation associated with COVID-19 may contribute to the development of Kounis syndrome by engendering a pro-inflammatory milieu, impairing myocardial function, and potentially exacerbating acute coronary events (3). There is a focus on ACS and COVID-19 vaccinations due to their cardiovascular risks. COVID-19 vaccinations prevent severe disease, hospitalization, and death; however, they can cause cardiovascular events like ACS. Unknown causes exist, but vaccine-induced immune responses may be responsible. ACS may be caused by immune system activation and inflammation, w hich d estabilize atherosclerotic plaques. A vaccine allergy could produce Kounis syndrome, a hypersensitivity-induced coronary artery spasm that could cause ACS. This is rare, and immunization benefits exceed concerns. Pre-existing cardiovascular conditions may increase risk, but causality is unclear. While promoting the

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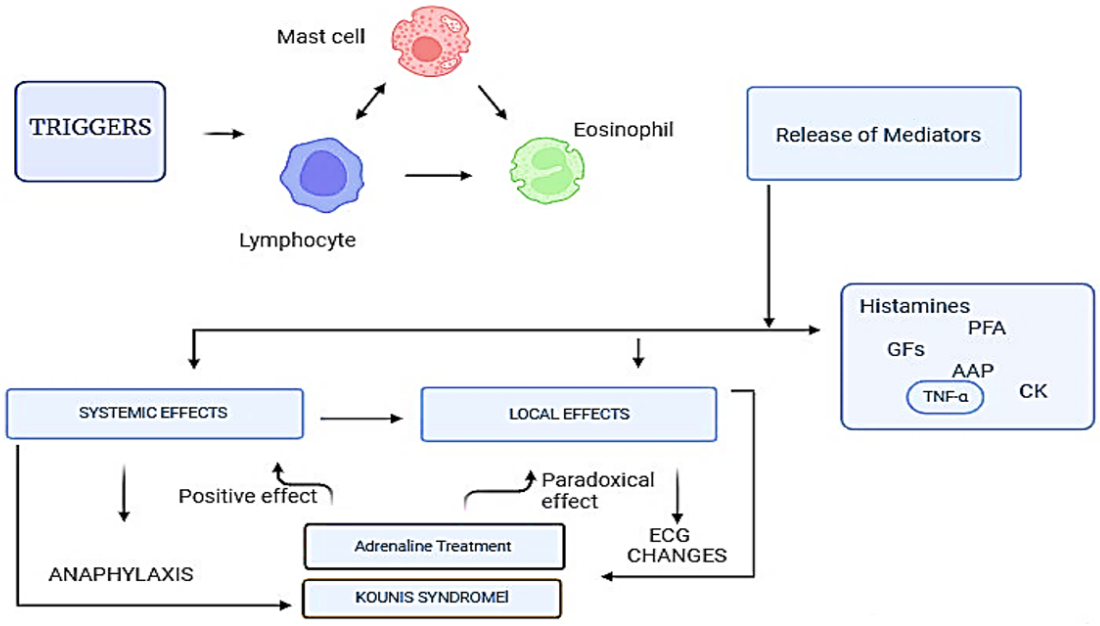

Figure 1 Pathophysiology of Kounis syndrome a flowchart

COVID-19 vaccination, healthcare practitioners must monitor and manage risks, especially for high-risk patients. Risk factors and molecular mechanisms of COVID-19 immunization and ACS need further study. This will help create vaccination strategies that reduce risks and improve safety for all populations (14,16).

5. Risk factors and predisposing conditions for Kounis syndrome in the context of COVID-19

Certain risk factors and predisposing conditions may increase the susceptibility to developing Kounis syndrome in individuals infected with SARS-CoV-2 (1,6). Patients with pre-existing cardiovascular diseases, such as coronary artery disease, heart failure, or valvular heart disease, may be at heightened risk. Additionally, individuals with a history of allergic or atopic conditions, including asthma, eczema, or hay fever, may be more prone to developing hypersensitivity reactions, potentially triggering Kounis syndrome (1). Furthermore, certain medications employed in the management of COVID-19, encompassing antivirals, antibiotics, or immunomodulatory agents, possess the potential to elicit allergic reactions and contribute to the development of Kounis syndrome (6). Age and the presence of comorbidities, such as diabetes mellitus, hypertension, and obesity, have been associated with more severe clinical manifestations of COVID-19 and an augmented risk of cardiovascular complications, (3,7) suggesting that these factors may also predispose individuals to the development of Kounis syndrome in the context of SARS-CoV-2 infection. Importantly, the interplay between these risk factors, COVID-19 pathophysiology, and the mechanisms underlying Kounis syndrome may culminate in a synergistic amplification of the inflammatory and thrombotic processes, potentially exacerbating the severity and adverse outcomes of acute coronary events (3). While there have been recorded instances of allergic reactions after immunisation, there is currently no established connection between COVID-19 and Kounis syndrome. Post-vaccination, there have been reports of Kounis syndrome, which is an allergic reaction that leads to ACS. The absence of reliable evidence creates uncertainty regarding the cause-and-effect relationship. Regrettably, there is no precise correlation between contracting COVID-19 and the occurrence of ACS, a crucial factor for diagnosing Kounis syndrome. Kounis syndrome occurs when a medication, insect sting, or vaccination causes ACS. The duration of ACS in relation to an allergic reaction or vaccination is often unpredictable in cases of COVID-19 infection. Several COVID-19 ACS patients do not exhibit any allergy or anaphylactic symptoms, which adds complexity to the situation. Urticaria, angioedema, and bronchospasm are immediate allergic responses observed in Kounis syndrome. The occurrence of Kounis syndrome in COVID-19-related ACS is improbable due to its infrequent manifestation of allergy symptoms. Kounis syndrome is characterised by an allergic reaction and the involvement of the coronary arteries. Consequently, the absence of symptoms further complicates the association with COVID-19 (15,16).

6. Clinical presentation and diagnosis

The clinical presentation of Kounis syndrome in the context of COVID-19 may vary depending on the underlying mechanisms and severity of the condition (1). Patients may present with symptoms suggestive of acute coronary syndrome, such

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as chest pain, shortness of breath, or electrocardiographic (ECG) changes indicative of myocardial ischemia or infarction (1). Additionally, they may exhibit signs and symptoms of an allergic or hypersensitivity reaction, including urticaria, angioedema, wheezing, or anaphylaxis (1). The diagnosis of Kounis syndrome in COVID-19 patients may be challenging due to overlapping clinical features and the potential for misdiagnosis (5). A thorough clinical history, including recent exposure to potential allergens or triggers, history of allergic reactions, and cardiovascular risk factors, should be obtained (1). Physical examination should assess for signs of allergic reactions and cardiovascular findings suggestive of myocardial ischemia or infarction. Diagnostic workup may involve ECG, measurement of cardiac biomarkers (troponin, CK-MB), coronary angiography in cases of suspected myocardial infarction, and an allergic workup (serum tryptase, IgE levels, skin testing) to identify potential triggers and confirm the allergic or hypersensitivity component (1).

Identification of inflammatory markers and cells in thrombotic lesions diagnoses Kounis syndrome, commonly known as allergic myocardial infarction. Kounis syndrome, caused by allergies or hypersensitivity, and ACS. This rare mix of immunological and cardiovascular issues necessitates a precise diagnosis. Increased circulating inflammatory mediators are the first sign of Kounis syndrome. During allergic reactions, inflammatory mediators such as histamine, tryptase, leukotrienes, interleukins (IL-4, IL-6, IL-10), and TNF- are released into the bloodstream. In Kounis syndrome, these substances increase and can cause coronary artery spasm, atherosclerotic plaque destabilization, and thrombosis.

Histological identification of inflammatory cells in thrombotic lesions is another Kounis syndrome diagnostic criteria. After death or biopsy, the coronary thrombus contains eosinophils, mast cells, macrophages, and other immune cells. Kounis syndrome is marked by cardiac thrombi with allergic cells. Kounis syndrome is characterized by allergic reactions (e.g., urticaria, angioedema, or anaphylaxis) with ACS symptoms such as chest discomfort, increased troponin, and ischaemia-related electrocardiograms. We must rule out non-allergic causes to confirm ACS. This involves a complete patient history, allergy testing, and other diagnostics. High inflammatory mediator levels, thrombotic lesions with inflammatory cells, and clinical signs diagnose Kounis syndrome. Due to the allergic component, this condition may require different therapy than conventional ACS regimens; hence, accurate identification is vital (17).

7. Differentiating Kounis syndrome from other COVID-19-related cardiovascular complications

The diagnosis of Kounis syndrome in COVID-19 patients should be made in the context of a thorough clinical evaluation and after ruling out other potential causes of acute coronary syndromes or myocardial injury (5). COVID-19 itself has been associated with various cardiovascular complications, including myocardial injury, arrhythmias, heart failure, and thromboembolic events (3). It is crucial to distinguish Kounis syndrome from the direct cardiovascular effects of COVID-19 or other potential causes, such as pre-existing cardiovascular disease or secondary complications of severe illness. The presence of an allergic or hypersensitivity component, along with the temporal association between the onset of symptoms and potential triggers, can assist in the diagnosis of Kounis syndrome (1).

8. Management and therapeutic considerations

A multifaceted approach combining cardiologists, allergists, and other pertinent experts is necessary for the therapy of Kounis syndrome in COVID-19 patients. Prompt removal of the allergen or trigger, if identified, is crucial in the acute treatment of allergic or hypersensitive reactions (8). When anaphylaxis or severe allergic reactions occur, it is critical to provide epinephrine very away. Moreover, the prudent application of antihistamines (which include H1 and H2 receptor antagonists), corticosteroids, and bronchodilators is necessary to reduce symptoms and the immune response. To effectively manage acute allergy episodes, a coordinated application of the managed therapeutic approaches is essential. According to Kounis et al. (2019), therapeutic protocols for the management of ACS must be followed religiously. These protocols call for the use of anticoagulation, antiplatelet therapy, and revascularization techniques like coronary artery bypass grafting or percutaneous coronary intervention whenever clinically indicated (9). Furthermore, evaluation of intracoronary vasodilators is necessary, especially when treating coronary artery spasms, and includes nitrates and calcium channel blockers (1). These therapies demonstrate the complex management strategy that is necessary for ACS, as explained in the current literature (9). Cardiovascular risk factor optimization is of utmost relevance when it comes to long-term management. This comprises the careful treatment of evidence-based pharmaceutical therapies and lifestyle adjustments for the underlying cardiovascular risk factors, such as diabetes, dyslipidaemia, and hypertension. These therapies include dietary changes, the adoption of structured exercise programs, and lifestyle improvements such as quitting smoking. These multifaceted strategies target specific risk factors as well as their interactions, working together to address them holistically to reduce cardiovascular morbidity and mortality. This all-encompassing strategy emphasizes the importance of incorporating lifestyle and medication modifications into the long-term management paradigm, as supported by recent review literature. For long-term care, careful detection and avoidance of allergens or other triggers that cause Kounis syndrome are essential, as is the continued use of statins, antiplatelet medicines, and customized cardiovascular drugs. Furthermore, individuals with recurring episodes of Kounis

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syndrome should take mast cell stabilizers or leukotriene inhibitors into account. Thorough monitoring for the return of the syndrome or the advancement of cardiovascular disease and close collaboration with cardiologists and allergists are crucial aspects of patient management. In the context of COVID-19, it is critical to follow recommended treatment protocols, which include antiviral therapy and careful monitoring for complications. It is necessary to be aware of any possible drug interactions between COVID-19 therapy and prescriptions for cardiovascular disease or Kounis syndrome. Encouraging interdisciplinary cooperation between cardiologists, allergists, infectious disease experts, and other pertinent medical personnel guarantees all-encompassing patient treatment.

9. Prognosis and future directions

The prognosis of Kounis syndrome in COVID-19 patients may vary depending on factors such as the severity of the acute coronary event, the presence of underlying cardiovascular disease, and the effectiveness of treatment (1). Prompt and appropriate management generally lead to a favourable prognosis and resolution of the acute coronary event, while pre-existing cardiovascular disease or complications like heart failure or arrhythmias can negatively impact the prognosis, further compounded by the increased risk of cardiovascular complications and potential long-term sequelae associated with COVID-19 itself, highlighting the need for careful monitoring and follow-up of these patients (2,3,13). Future research directions in this area may include epidemiological studies to determine the incidence, prevalence, risk factors, and predisposing conditions; investigations into pathophysiological mechanisms, including viral entry and receptor interactions, experimental models and in vitro studies, and animal models; biomarker studies for predicting Kounis syndrome development; genetic and genomic studies to identify potential predispositions; clinical trials evaluating therapeutic interventions; long-term follow-up studies assessing cardiovascular outcomes and prognosis; application of artificial intelligence and machine learning for early detection, risk stratification, and management; and fostering multidisciplinary collaborations between cardiologists, allergists, infectious disease specialists, immunologists, and other relevant experts to advance understanding and develop integrated management strategies.

10. Conclusion

The combination of Kounis syndrome with COVID-19 poses an intricate therapeutic challenge. The association between Kounis syndrome, a rare illness that connects allergic reactions to acute coronary crises, and COVID-19 is still uncertain. While case reports indicate a possible connection between COVID-19 vaccination and Kounis syndrome, there is currently no conclusive data available. The inflammatory nature of COVID-19 may worsen the underlying causes of Kounis syndrome, however the specific aetiology is still unknown. Furthermore, the lack of rapid allergy responses in numerous instances of COVID-19 makes identification and treatment more challenging. In order to tackle these difficulties, it is crucial to adopt a multidisciplinary strategy. Future study should investigate the fundamental principles, discover biomarkers, and create effective treatment techniques to enhance patient outcomes. In order to provide the best possible care for patients who are at risk of developing Kounis syndrome during the continuing pandemic, it is essential to have a thorough awareness of the intricate relationship between many factors involved.

11. Declarations

11.1. Acknowledgement

The authors have no acknowledgments to declare.

11.2. Authors' contribution

The idea for the manuscript was conceived by Abinavi Balaji. Abinavi Balaji scripted and worked extensively on the entire paper. Vinod Kumar Kaluram provided inputs in citing references and contributed to the writing, reviewing, and approval processes. All authors were involved in the writing, critical review, and final approval of the manuscript.

11.3. Conflict of interest

None.

11.4. Funding

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References

1. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis, and therapeutic management. Clin Chem Lab Med. 2016;54(10):1545-59.
2. basic mechanisms to clinical perspectives. Nature reviews Cardiology. 2020;17(9):543-58.
3. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. J Am Coll Cardiol. 2020;75(18):2352-71.
4. Babapoor-Farrokhran S, Gill D, Walker J, Rasekhi RT, Bozorgnia B, Amanullah A. Myocardial injury and COVID-19: possible mechanisms. Life Sci. 2020;253:117723.
5. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? Int J Cardiol. 2006;110(1):7-14.
6. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and

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treatment options. Cardiovasc Res. 2020;116(10):1666-87.
7. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020;94:91-5..
8. Kounis NG. Coronary hypersensitivity disorder: the Kounis syndrome. Clin Ther. 2013;35(5):563-71.
9. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Jr., Ganiats TG, Holmes DR, Jr., et al. 2014 AHA/ACC Guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64(24):e139-e228.
10. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17(5):259-260.
11. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC State-of-the-Art Review. J Am Coll Cardiol. 2020;75(23):2950-73.
12. Chen C, Zhou Y, Wang DW. SARS-CoV-2: a potential novel etiology of fulminant myocarditis. Herz. 2020;45(3):230-2.
13. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature. 2020;584(7821):430-6.
14. Memon S, Chhabra L, Masrur S, Parker MW. Allergic acute coronary syndrome (Kounis syndrome). Proc (Bayl Univ Med Cent). 2015;28(3):358-62.
15. Sahraian S, Eshaghian S, Houshmand G, Emamzadeh A, Akbari R. Kounis syndrome in a patient with COVID-19: a case report. J Investig Med High Impact Case Rep. 2021;9:232470962110085.
16. Zhao C, Lei R, Liu S, Zhao M. Kounis syndrome following COVID-19 vaccination: clinical manifestations, mechanisms and management. Hum Vaccin Immunother. 2024;20(1):2365496.
17. Paknahad MH, Yancheshmeh FB, Soleimani A. Cardiovascular complications of COVID-19 vaccines: a review of case-report and case-series studies. Heart & Lung. 2023;59:173-80.
18. Wang L, Tang C. Targeting platelet in atherosclerosis plaque formation: current knowledge and future perspectives. International journal of molecular sciences. 2020;21(24):9760.

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