Invited lecture/Review

Cardiac Arrhythmias in Patients with Myocarditis in the Post-COVID-19 Period

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Abstract:

To date, several cardiotropic viruses have been implicated as causes of myocarditis. The most detected are parvovirus B19, and human herpes virus 6. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) are the respiratory viruses that have recently triggered the unprecedented pandemic process. The involvement and impact of these viruses in viral cardiovascular disease are under study. Despite extensive research into the pathological mechanisms of viral infections of the cardiovascular system, our knowledge regarding their treatment and management is still incomplete. A condition caused by post- Co rona Virus Disease (COVID-19) myocarditis seems to have distinct inflammatory characteristics. Many kinds of arrhythmias may occur in patients with post-COVID-19 myocarditis and result in arrhythmogenic cardio-myopathy and sudden cardiac death. Sometimes arrhythmia can be the first and only symptom of myocarditis. However, compared to the other clinical presentations, arrhythmic myocarditis has been poorly described in the literature. The increased risk of arrhythmias in patients with a post-COVID-19 period is most likely a consequence of systemic inflammation and diseases, not just a direct consequence of the viral infection. A decrease in heart rate variability can contribute to electrical instability of the myocardium and the occurrence of arrhythmias. Cardiac magnetic resonance imaging and endomyocardial biopsy are the most useful tests for myocarditis. However, different from the other clinical presentations, arrhythmic myocarditis requires specific diagnostic, prognostic, and therapeutic considerations. This review aims to critically summarize the state of the art on myocarditis presenting with arrhythmias in terms of epidemiology, aetiology, diagnosis, prognosis, and treatment.

Keywords: Post-COVID-19; SARS-CoV-2; Myocarditis; Arrhythmias; Ferroptosis; Vaccination

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1. Introduction

Since December 2019, the novel coronavirus SARS-CoV-2 has spread rapidly throughout China and still keeps the world in suspense. Cardiovascular complications with myocarditis and embolism due to COVID-19 have been reported. SARS-CoV-2 genome detection in the heart muscle has not been demonstrated so far, and the underlying pathophysiological mechanisms remain to be investigated.

Myocarditis is described as an inflammation of the heart muscle, resulting in damage in the absence of ischemia. It has been suggested that viruses are an important aetiology of myocarditis with a wide range of causes including but not limited to adenovirus, parvovirus B19, Epstein-Barr virus and cytomegalovirus (Siddiqi et al., 2021). Now the latest evidence suggests that SARS-CoV-2 virus may also be an important infectious agent for myocarditis. The proposed pathophysiology of viral myocarditis is a combination of direct cellular damage and immune-mediated cell death. Many kinds of arrhythmias may occur in patients with post-COVID- 19 myocarditis and develop into arrhythmogenic cardiomyopathy and sudden cardiac death (Chung et al., 2021).

2. SARS-CoV-2 and Myocarditis

COVID-19 can lead to subacute and chronic myocarditis of varying severity. Post-COVID myocarditis is characterized by prolonged persistence of coronavirus in combination with high immune activity (high titres of antinuclear antibody), which should be considered as the main mechanisms of its long-term course (Ali et al., 2022).

The incidence of COVID-19-induced myocarditis is not well established. A study reported that myocardial injury occurred in 20% to 30% of hospitalized patients with COVID-19 infection, and cardio-vascular complications contributed to approximately 40% of all COVID-19–related deaths (Ismayl et al., 2022).

During March 2020–January 2021, patients with COVID-19 had nearly 16 times the risk for myocarditis compared with patients who did not have COVID-19, and risk varied by sex and age (Boehmer et al., 2021).

In a study conducted in Germany (Escher et al., 2020), endomyocardial biopsies were performed on 104 patients with acute myocarditis and heart failure who had been infected with COVID-19. The study showed that SARS-CoV-2, as detected by PCR, was present in only 5% of patients. However, genomes of other viruses were detected in 85% of cases, the most frequently detected was Parvovirus B 19 (Escher et al., 2020). The authors suggested that SARS-CoV-2 in many cases could be the trigger that led to the development of inflammatory damage of the myocardium (Escher et al., 2020).

Later, in 2021, a review was published that included more than 1,000 patients with suspected acute myocarditis and heart failure, and SARS-CoV-2 genome was present in only 1% of the patients. The virus that appeared in 2019 is not a new cardiotropic virus. Thus, two large studies showed that in the case of myocarditis there were two viruses - one that was latent and the other that was replicating. Myocarditis can occur under the simultaneous influence of two or more different infections, when one of them, as a rule, creates conditions and the other is the direct cause of damage. It is not known whether clinical symptoms of cardiac histopathology differentiate patients with multiple infections or whether they have a worse prognosis compared to patients with only one type of virus in the heart. It should be noted that 90% of people have a latent virus in their blood at the end of their lives (Schultheiss et al., 2021).

In another study in Germany (Tanacli et al., 2021), Cardiac Magnetic Resonance (CMR) and EndoMyocardial Biopsy (EMB) findings revealed that a SARS CoV- 2 infection showed a variable cardiac involvement. Patients with more symptoms and those with higher clinical care demands were more likely to exhibit impaired myocardial function and developed chronic inflammation more often compared to patients with “classic” acute myocarditis during the acute and convalescent phases (Tschöpe et al). This study highlighted the importance of collecting large multicentre cardiac imaging data from patients with COCID-19 and patients recovering from COVID-19.

3. Vaccination and COVID-19

As for vaccination during COVID-19, there were doubts that the vaccination itself may have caused myocardial infarction and other heart complications. The analysis showed that such complications were very rare, i.e. 3 cases per 100,000, while the development of myocarditis in people without COVID-19 vaccination reached 11 per 100,000 (Barda et al., 2021). A population-based study quantified for the first time the risk of several rare cardiac adverse events associated with three COVID-19 vaccines as well as SARS-CoV-2 infection.

Vaccination for SARS-CoV-2 in adults was associated with a small increase in the risk of myocarditis within a week of receiving the first dose of both adenovirus and mRNA vaccines, and after the second dose of both mRNA vaccines. By contrast, SARS-CoV-2 infection was associated with a substantial increase in the risk of hospitalization or death from myocarditis, pericarditis and cardiac arrhythmia (Patone et al.,2022).

These findings underscore the importance of implementing evidence-based COVID-19 prevention strategies, including vaccination, to reduce the public health impact of COVID-19 and its associated complications.

4. Presentation of COVID-19 myocarditis

Presentation of COVID-19 myocarditis can vary from mild to severe (stated as dyspnea, fatigue, fever, cough, and chest pain). These symptoms are commonly seen in infections with previous phylogenetic viral groups such as SARS-COV or MERS-COV, in the presence or absence of myocarditis. Other symptoms listed are diarrhea, muscle pain, headaches, nausea and vomiting. The respiratory presentation gets further complicated with pre-existing risk factors due to congenital or heart conditions such as myocardial infarction, arrhythmia etc. Increased levels of cardiac biomarkers, electrocardiogram (ECG) findings (i.e. prolongation of the QT interval), non-specific ST-segment and T-wave changes and brady/tachyarrhythmia can be found (Pourfridoni et al., 2022). Global hypokinesis and pericardial effusion can be seen on echocardiography (Kermani-Alghoraishi et al., 2021). Myocardial fibrosis associated with arrhythmia can result in increased septal wall thickness (Ali et al., 2022).

5. Diagnostics of COVID-19 associated myocarditis

Blood test markers that are nonspecific and indicate signs of infection have been noted in COVID-19-associated myocarditis. These markers include Lactate DeHhydrogenase (LDH), white blood cell count and C-reactive protein (CRP). Apart from these, cardiac enzyme (e.g., creatine kinase - myoglobin binding (CK-MB), pro B type natriurec peptide (pro-BNP) and troponin levels have been found elevated (Kaufmann et al., 2022). But in spite of their normal levels, the presence of myocarditis was not necessarily excluded, therefore initial non-invasive investigations were found essential (Escher et al., 2020). ECG parameters like ST-T wave changes, QT prolongation, bradyarrhythmia and tachyarrhythmias are nonspecific since these are also found in other diseases of the heart. ECG can assess hypokinesia of the myocardial wall and rule out other valvular conditions and congenital malformations (Schultz et al., 2009). 2-D echocardiography lacks sensitivity and specificity in terms of identifying systolic and diastolic functioning variations (Sawalha et al., 2021). Computer Tomography (CT) offers better spatial resolution and due to its short acquisition time, it is useful in identifying fibrosis and abnormalities of cardiac wall motion, but it is being used for delayed enhancement (Chen and Jeudy, 2019). Nevertheless, EMB, it is the gold standard for confirmation of myocardial inflammation or fibrosis (Tavazzi et all., 2020). On the other hand, EMB carries a significant risk of arrhythmias, bleeding, nerve or vascular complications, perforation and pneumothorax (Mandoli et al., 2021). "Lake Louise Criteria" should be considered while interpreting CMR images (Cundari et al., 2021). CMR which uses T2-weighted, early and late gadolinium enhancement was suggested to be the best non-invasive technique as regards sensitivity (Puntmann et al., 2018) but failed to identify the aetiology (viral or autoimmune) so in this case, EMB could be a better choice (Chu et al., 2013). Ongoing developments are seeking for more objective, quantitative tissue markers for inflammation and necrosis or scar, and semiautomatic algorithms for image acquisition and evaluation (Chen and Jeudy, 2019).

6. Arrhythmias in post-COVID-19.

Arrhythmia can be the first and only symptom of myocarditis (Blagova et al., 2021). If the patient suddenly develops an arrhythmia of unknown origin, a possibility of myocarditis can be taken into account (Li et al., 2020). Development of arrhythmia at different stages of development of myocarditis corresponds to different mechanisms (Li et al., 2020). It was suggested that an increased risk of arrhythmias in patients with COVID-19 is most likely a consequence of systemic diseases, not just a direct consequence of the viral infection (Akkawi and Ghazal, 2021).

In 2020, a large study within European countries in the time interval of seven months showed that in many patients, the symptoms connected to COVID-19 persisted (mainly cardiac symptoms: chest pain and or tightness in the chest, shortness of breath, fatigue, sleep disturbance, night apnea, tachycardia, bradycardia) (Davis et al., 2021). The patients had not returned to previous levels of work and continued to experience significant symptom burden (Davis et al., 2021).
According to the current literature, we can find the following arrhythmogenic hypothetic mechanisms in the acute phase of viral myocarditis:

i. Direct cytopathic effect, which leads to electrical instability due to lysis of myocyte membranes (Agol, 2012).

ii, Ischemia as a result of a coronary macro-or microvascular lesion, for example, in viruses with endothelial tropism (Paravirus B 19) as a result of P antigen-mediated dysfunction of the endothelium (Petersen and Pepine, 2015)

iii, Dysfunction of the intercellular gap junction (gap junction dysfunction) due to impaired connexin expression in the myocardium, as shown in coxsackie virus-induced myocarditis in animal models (Hesketh et al., 2009)

iv, Disturbance of calcium transport and the functioning of ion channels, especially in myocarditis due to overlap with arrhythmic cardiomyopathy or channelopathies (Shah et al., 2006).

A possible explanation for why patients with COVID -19 report heart rhythm disturbances (tachy- or bradycardia) is SARS-CoV-2 infection of the pacemaker cells of the sinoatrial node, which leads to a marked increase in ferroptosis (Nishiga et al., 2022). Ferroptosis (English: ferroptos) is a type of programmed oxidative necrotic cell death, a characteristic feature based on the iron-dependent peroxidation of lipids. On experimental basis, deferoxamine and imatinib were found to block ferroptosis associated with SARS-CoV-2 infection (Han et al., 2022).

The studies on arrhythmias after COVID 19 myocarditis are very few. Arrhythmia specification of post-COVID-19 myocarditis was performed at Strazhesko Cardiology Institute of Ukraine (Kovalenko et al., 2020). The first group included patients with acute myocarditis and COVID-19 infection in anamnesis (n=25, male 53%, female 47%, age 35,3 ± 2,5 years) and the second group included patients with myocarditis without COVID-19 infection in anamnesis and negative polymerase chain reaction (PCR) (n=20, male 60% female 40%, age 34,9 ± 2,3 years). The diagnosis of acute myocarditis was established based on current recommendations with cardiac magnetic resonance imaging. In the first group, there was a significantly higher number of ventricular extrasystoles (VE) (53%), supraventricular extrasystoles SE (25%), paired VEs (by 27%), and episodes of ventricular allorhythmia (12%) compared to the second group (Kovalenko et al., 2020). Ventricular and supraventricular arrhythmias were observed more often in patients with myocarditis who suffered from COVID – 19, regardless of gender.

MRI in patients of the first group showed a larger volume of inflammatory and fibrotic lesions of the left ventricle (LV), which was evidenced by a larger number of LV segments in which both inflammatory changes and delayed contrast were detected (Kovalenko et al., 2020). In most cases, patients with a history of COVID - 19 infection had more damage to the ventricular septum (Kovalenko et al., 2020). From the data of this study, it could be

deduced that that fibrotic changes which developed during myocarditis were correlated with the number of supraventricular and ventricular arrhythmias (Kovalenko et al., 2020). It was suggested that supraventricular arrhythmia developed more often due to inflammatory processes and ventricular extrasystoles developed more often due to fibrotic damage (Kovalenko et al., 2020). In patients from group 1, damaged posterior and lateral walls of the left ventricle were correlated with supraventricular extrasystoles while damaged ventricular septum was correlated with ventricular extrasystoles and supraventricular tachycardia (Kovalenko et al., 2020).

In a study performed in Tbilisi in 2022, the assessment of cardiac autonomic imbalance was based on heart rate measurements obtained during 24-hour Holter monitoring (Malidze et al., 2022). Parameters of Heart rate Variability (HRV) were assessed in 2 groups randomized with respect to age and gender. The 1st group included patients with acute myocarditis after COVID -19 infection, and the second group included patients with acute myocarditis without COVID 19 infection in anamnesis, which was confirmed by negative serological studies. Patients were not vaccinated against COVID -19. A more pronounced decrease in the activity of the parasympathetic peripheral nervous system of the heart rhythm was revealed in patients who had COVID -19 infection, standard deviation normal to normal intervals (SDNN), 103 ± 25 ms vs 128 ± 32 ms, $p < 0.001$ and high frequency (HF), 235 ± 198 ms vs 473 ± 179 ms, $p < 0.001$) (Malidze et al., 2022).

It was suggested that impairment of sympathetic-vagal balance of the heart rhythm regulation lowers the excitability threshold of cardiac cells in post-COVID syndrome patients and can contribute to the development of the electrical instability of the myocardium and the occurrence of arrhythmias (Malidze et al., 2022).

7. Treatment of COVID-19-associated myocarditis

Corticosteroids in addition to antiviral therapy, colchicine, immunoglobulins and immuno-modulators have decreased mortality rates in patients with or without pre-existing comorbidities (Feuillet et al., 2021). Current research indicates that the effect of corticosteroids hydrocortisone and oral prednisone is on immune system since increased amounts of cytokines and chemokines have been detected in patients with multiple organ dysfunction related to SARS-CoV-2 (Kamarullah et al., 2021).

Positive chronotropic (e.g. dopamine) agents are considered for atrioventricular block, instead of the transvenous pacemaker to minimize personal protective equipment use and healthcare worker's risk (Limanaqi et al., 2022). It was suggested to postpone permanent pacemaker implantation to allow for an improvement of bradycardia (Kochav et al., 2020).

For atrial fibrillation in stable patients in the absence of heart failure, rate control and anticoagulation are suggested while in hemodynamically unstable patients, urgent cardioversion was found necessary (Holt et al., 2020). Apart from this, calcium channel blockers or digoxin and beta blockers have been used for controlling conduction through the atrioventricular node (Holt et al., 2020). To assess left atrial appendage thrombus, CT angiography was suggested instead of Transoesophageal Echocardiography (TEE) due to the risk of viral aerosolization (Hu et al., 2020). It is still unclear how long systemic anticoagulation should be used for prothrombotic state associated with severe viral infection (Kochav et al., 2020). Clinicians or healthcare workers should consider drug-drug interactions while giving antivirals to prevent unnecessary side effects or toxicity. It was reported that amiodarone has been used for a short time in a patient with hypertension and cardiomyopathy (Hu et al., 2020). Depending upon the patient's risk profile, anticoagulation was recommended while the patient was being monitored (Hu et al., 2020). Cardiac troponin measurement and an echocardiogram were suggested for further evaluation (Hu et al., 2020). QT corrected (QTc) interval - prolonging drugs (e.g., hydroxychloroquine) were found to trigger arrhythmias (Lewis et al., 2020) which should be taken into account. To avoid polymorphic ventricular tachycardia and pulseless electrical activity, potassium and magnesium deficiency should be monitored and repleted (Kochav et al., 2020). Defibrillation was suggested as an option for sustained arrhythmias of ventricles (Hu et al., 2020). Implantation of cardioverter-defibrillator (ICD) for secondary prevention was suggested in patients with myocarditis and symptomatic ventricular arrhythmias, especially if these persisted after the acute phase despite pharmacotherapy (Hu et al., 2020). However, the

timing of implanting ICD remains unclear (Wadhwani et al., 2021). Implantation of a cardiac device for the treatment of ventricular arrhythmias (VA) is indicated 3-6 months after the acute phase (Wadhwani et al., 2021). Body-worn external cardioverter defibrillator has been considered in patients at high risk of sudden death, patients with lymphocytic myocarditis, and patients with myocarditis and ventricular arrhythmias in the acute phase of the disease (Wadhwani et al., 2021). However, the best terms for its use have not been prospectively investigated (Dherange et al., 2020).

Conclusions

The incidence of COVID-19-induced myocarditis and it's mortality is not well established. In patients with myocarditis, in any phase of the disease, complex and heterogeneous arrhythmias can occur, which vary from conduction system disturbances of the heart to life-threatening ventricular tachycardia and ventricular fibrillation. Myocarditis is often underdiagnosed, and the occurrence of arrhythmia may be a sign of its debut. Myocarditis with heart rhythm and conduction system disturbances requires specific diagnostic imaging methods for choosing treatment tactics

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References

1. Agol VI. Cytopathic effects: virus-modulated manifestations of innate immunity? Trends in Microbiology. 2012; 20(12): 570–576. DOI: 10.1016/j.tim.2012.09.003
2. Akkawi AR, Ghazal M. COVID-19 and Cardiac Arrhythmias: A Review of the Literature. Cureus. 2021; 13: e17797. DOI: 10.7759/cureus.17797
3. Ali MS, Shiwani HA, Elfaki MY, et al. COVID-19 and myocarditis: a review of literature. Egypt Heart J. 2022; 74: 23. DOI: 10.1186/s43044-022-00260-2
4. Barda N, Dagan N, Ben-Shlomo Y, et al. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. N Engl J Med. 2021; 385: 1078-1090. DOI: 10.1056/NEJMoa2110475
5. Blagova OV, Varionchik, NV, Zaidenov VA, et al. Previous and First Detected Cardiovascular Diseases in Patients with New Coronavirus Pneumonia: Possible Mechanisms and Place in a Unified Prognostic Model. Int Arch Allergy Immunol. 2021; 182: 765–774. DOI: 10.1159/000515253
6. Boehmer TK, Kompaniyets L, Lavery AM, 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: 1228-1232. DOI: 10.15585/mmwr.mm7035e5
7. Chen W, Jeudy J. Assessment of Myocarditis: Cardiac MR, PET/CT, or PET/MR? Current Cardiology reports. 2019; 21(8): 76. DOI: 10.1007/s11886-019-1158-0
8. Chu GC, Flewitt JA, Mikami Y, et al. Assessment of acute myocarditis by cardiovascular MR: diagnostic performance of shortened protocols. Int J Cardiovasc Imaging. 2013; 29: 1077-1083. DOI:10.1007/s10554-013-0189-7
9. Chung MK, Zidar DA, Bristow MR, et al. COVID-19 and cardiovascular disease: from bench to bedside. Circ Res. 2021; 128: 1214–1236. DOI: 10.1161/CIRCRESAHA.121.317997
10. Cundari G, Galea N, De Rubeis G, et al. Use of the new Lake Louise Criteria improves CMR detection of atypical forms of acute myocarditis. Int J Cardiovasc Imaging. 2021; 37: 1395-1404. DOI: 10.1007/s10554-020-02097-9
11. Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine. 2021; 38:101019. DOI: 10.1016/j.eclinm.2021.101019
12. Dherange P, Lang J, Qian P, et al. Arrhythmias and COVID-19: A Review. JACC Clin Electrophysiol. 2020; 6: 1193-1204. DOI: 10.1016/j.jacep.2020.08.002
13. Escher F, Pietsch H, Aleshcheva G, et al. Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. ESC Heart Fail. 2020; 7: 2440-2447. DOI: 10.1002/ehf2.12805
14. Feuillet V, Canard B, Trautmann A. Combining Antivirals and Immunomodulators to Fight COVID-19. Trends in immunology. 2021; 42: 31–44. DOI: 10.1016/j.it.2020.11.003
15. Han Y, Zhu J, Yang L, et al. SARS-CoV-2 Infection Induces Ferroptosis of Sinoatrial Node Pacemaker Cells. Circ Res. 2022; 130: 963-977. DOI: 10.1161/CIRCRESAHA.121.320518

16. Hesketh GG, Van Eyk JE, Tomaselli GF. Mechanisms of gap junction traffic in health and disease. Journal of cardiovascular pharmacology. 2009; 54: 263–272. DOI: 10.1097/FJC.0b013e3181ba0811
17. Holt A, Gislason GH, Schou, et al. New-onset atrial fibrillation: incidence, characteristics, and related events following a national COVID-19 lockdown of 5.6 million people. European heart journal. 2020; 41: 3072–3079. DOI: 10.1093/eurheartj/ehaa494
18. Hu YF, Cheng WH, Hung Y, et al. Management of Atrial Fibrillation in COVID-19 Pandemic. Circulation journal : official journal of the Japanese Circulation Society. 2020; 84: 1679–1685. DOI: 10.1253/circj.CJ-20-0566
19. Ismayl M, Abusnina W, Thandra A, et al. Delayed acute myocarditis with COVID-19 infection. Proc (BAYL Univ Med Cent). 2022; 35: 366–368. DOI: 10.1080/08998280.2022.2030189
20. Kaufmann CC, Ahmed A, Burger AL, et al. Biomarkers Associated with Cardiovascular Disease in COVID-19. Cells. 2022; 11: 922. DOI: 10.3390/cells11060922
21. Kamarullah W, Nurcahyani, Mary Josephine C, et al. Corticosteroid Therapy in Management of Myocarditis Associated with COVID-19; a Systematic Review of Current Evidence. Arch Acad Emerg Med. 2021; 9: e32. DOI: 10.22037/aaem.v9i1.1153
22. Kermani-Alghoraishi M, Pouramini A, Kafi F, Khosravi A. Coronavirus Disease 2019 (COVID-19) and Severe Pericardial Effusion: From Pathogenesis to Management: A Case Report Based Systematic Review. Current problems in cardiology. 2022; 47: 100933. DOI: 10.1016/j.cpcardiol.2021.100933
23. Kochav SM, Coromilas E, Nalbandian A, et al. Cardiac Arrhythmias in COVID-19 Infection. AHA Journals. Circ: Arrhythmia and Electrophysiology. 2020; 13: 6. DOI: 10.1161/CIRCEP.120.008719
24. Kovalenko VN, Nesukay EG, Kornienko TM, Titova NS. COVID-19 Pandemic and Cardiovascular Disease Ukrainian Journal of Cardiology. 2020; 27: 10–17. DOI: 10.31928/1608-635X-2020.2.1017
25. Lewis J, Gregorian T, Portillo I, Goad J. Drug interactions with antimalarial medications in older travelers: a clinical guide. Journal of Travel Medicine. 2020; 27: taz089. DOI: 10.1093/jtm/taz089
26. Limanaqi F, Zecchini S, Dino B, et al. Dopamine Reduces SARS-CoV-2 Replication In Vitro through Downregulation of D2 Receptors and Upregulation of Type-I Interferons. Cells. 2022; 11:1691. DOI: 10.3390/cells11101691
27. Li X, Pan X, Li Y, et al. Cardiac injury associated with severe disease or ICU admission and death in hospitalized patients with COVID-19: a meta-analysis and systematic review. Critical care (London, England). 2020; 24: 468. DOI: 10.1186/s13054-020-03183-z
28. Malidze D, Noniashvili M. Accelerated heartbeat in post covid syndrome:what is behind it? XXIII National Congress of cardiologist of Ukraine, 22.09.2022. Accessed at https://cardiocongress.org.ua/#online
29. Mandoli GE, D'Ascenzi F, Vinco G, et al. Novel Approaches in Cardiac Imaging for Non-invasive Assessment of Left Heart Myocardial Fibrosis. Frontiers in Cardiovascular Medicine. 2020; 8: 614235. DOI: 10.3389/fcvm.2021.614235
30. Nishiga M, Jahng JWS, Wu JC. Ferroptosis of Pacemaker Cells in COVID-19. Circulation Research, 2022; 13: 978–980. DOI: 10.1161/CIRCRESAHA.122.320951
31. Patone M, Mei XW, Handunnetthi L, et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nat Med. 2022; 28: 410-422. DOI: 10.1038/s41591-021-01630-0
32. Petersen JW, Pepine CJ. Microvascular coronary dysfunction and ischemic heart disease: where are we in 2014? Trends in Cardiovascular Medicine. 2015; 25: 98–103. DOI: 10.1016/j.tcm.2014.09.013
33. Pourfridoni M, Khan MAB, Khalil-Khan A, et al. Elevated troponin level and nonspecific ST-segment and T-wave changes in a suspected acute pancreatitis patient, post-SARS-Cov-2 infection: A case report. Clinical Case Reports. 2022; 10: e6628. DOI: 10.1002/ccr3.6628
34. Puntmann VO, Zeiher AM, Nagel E. T1 and T2 mapping in myocarditis: seeing beyond the horizon of Lake Louise criteria and histopathology. Expert Rev Cardiovasc Ther. 2018; 16: 319-330. DOI: 10.1080/14779072.2018.1455499
35. Sawalha K, Abozenah M, Kadado AJ, et al. Systematic review of COVID-19 related myocarditis: insights on management and outcome. Cardiovascular Revascularization Medicine. 2021; 23: 107-113. DOI: 10.1016/j.carrev.2020.08.028
36. Schultheiss HP, Baumeier C, Pietsch H, Bock CT,et al. Cardiovascular consequences of viral infections: from COVID to other viral diseases. Cardiovascular Research. 2021; 117: 2610–2623. DOI: 10.1093/cvr/cvab315
37. Schultz JC, Hilliard AA, Cooper Jr LT, Rihal CS. Diagnosis and treatment of viral myocarditis. Mayo Clin Proc. 2009; 84: 1001-1009. DOI: 10.1016/S0025-6196(11)60670-8
38. Shah VN, Chagot B, Chazin WJ. Calcium-Dependent Regulation of Ion Channels. Calcium Binding Proteins. 2006; 1: 203–212.
39. Siddiqi HK, Libby P, Ridker PM. COVID-19 – A vascular disease. Trends Cardiovasc Med. 2021; 31: 1-5. DOI: 10.1016/j.tcm.2020.10.005

40. Tanacli R, Doeblin P, Götze C, Zieschang V, Faragli A, Stehning C, et al. COVID-19 vs. Classical Myocarditis Associated Myocardial Injury Evaluated by Cardiac Magnetic Resonance and Endomyocardial Biopsy. Front Cardiovasc Med. 2021; 8: 737257. DOI: 10.3389/fcvm.2021.737257
41. Tavazzi G, Pellegrini C, Maurelli M, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. European Journal of Heart Failure. 2020; 22: 911-915. DOI: 10.1002/ejhf.1828
42. Tschöpe C, Ammirati E, Bozkurt B, et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nature Reviews Cardiology. 2021; 18: 169-193. DOI: 10.1038/s41569-020-00435-x
43. Wadhwani L, Occhipinti K, Selim A, et al. Time to diagnosis of acute complications after cardiovascular implantable electronic device insertion and optimal timing of discharge within the first 24 hours. Heart Rhythm. 2021; 18: 2110–2114. DOI: 10.1016/j.hrthm.2021.09.008