LESION OF THE CARDIOVASCULAR SYSTEM IN POST-COVID SYNDROME

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Abstract:*Post-COVID syndrome (PCS) is a multisystem detection of survivors of novel coronavirus infection (NCVI) which develop symptoms after 12 weeks or more. PCS can be regardless of the severity of the disease. Lasts from several weeks to months. Manifestations of PCS capture various body systems, including the cardiovascular system (CVS).*

Purpose of the study. Based on the data of scientific medical literature, reading of changes, normalization in the cardiovascular system with PCS.

Materials and methods. bibliographic method. 23 sources of foreign and domestic scientific medical literature were analyzed.

Keywords:*Post-COVID syndrome, Novel Coronavirus Infection, Cardio-vascular system, Pericarditis, Treatment, Inflammation, Symptoms, Quality of life.*

INTRODUCTION

COVID-19 is a novel disease caused by the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). Since its first description in December 2019, COVID-19 progressed into a major public health concern. Patients suffered from symptoms such as fever, dry cough, and fatigue, which is mild in about 80% of cases; however, the severity may progress to develop respiratory distress. Recovery from COVID-19 occurs within 7–10 days in mild disease; it could take 3–6 weeks in severe illnesses. According to the Centers for Disease Control and Prevention, post-COVID-19 conditions are a wide range of new, returning, or ongoing health problems that people can experience for more than 4 weeks after initially being infected with the virus that causes COVID-19. Even asymptomatic can have post-COVID-19 conditions. These conditions are multisystem illnesses with different types and combinations of health problems for varying lengths of time and manifestations differ between patients and within patients over time. Follow-up of patients who recovered showed that one or more symptoms persist in a substantial percentage of people, even weeks or months after COVID-19. A study done in Egypt revealed that only 10.8% of all subjects had no residual symptoms after recovery; however, a major proportion suffered from several symptoms and diseases.

COVID-19 and the cardiovascular system

The primary target for SARS-CoV-2 is the respiratory tract, but the cardiovascular system can be involved too.

As well as the mild flu-like symptoms, COVID-19 often causes serious damage to the cardiovascular system - pulmonary vascular endothelialitis, microangiopathy, diffuse thrombosis, cardiac arrhythmias, heart failure, myocarditis, pericarditis and acute coronary syndromes.

Once in the nasopharynx, the SARS-CoV-2 enters the body by binding through its S-binding protein to angiotensin I-converting enzyme 2 (ACE2) receptors, found mainly in the lungs, cardiac myocytes, and endothelial cells in the vessel wall.

ACE2 is known to have protective effects by counteracting angiotensin II and over activating renin-angiotensin-aldosterone system (RAAS), which occurs in conditions of cardiovascular disease (CVD) such as hypertension, congestive heart failure and atherosclerosis.

Entering through endocytosis, this RNA virus begins to replicate, causing widespread infection. Since ACE2 converts angiotensin I and II to cardioprotective peptides - angiotensin 1-9 and angiotensin 1-7, its loss on cell surface may potentiate cardiac damage, resulting in endothelial dysfunction, inflammation and thrombosis.

ACE2 activity is known to be reduced in vessels with established atherosclerotic plaques and diabetes, while it is increased in women and young people due to the action of estrogens.

Decreased ACE2 activity may potentiate the so-called cytokine storm. This is an overreaction of the immune system caused by dysregulating RAAS and activating ACE2/bradykinin axis. The overproduction of cytokines and hyperinflammation leads to exacerbation of underlying cardiovascular diseases or triggering new ones.

According to the latest epidemiological data, about 80% of patients with COVID 19 have mild symptoms, about 45% have symptoms requiring hospitalization, while 5% of patients need mechanical ventilation . The difference in course is related to the degree of viral load, host immune response, age of the patient and the presence of concomitant diseases such as hypertension, diabetes and coagulation abnormalities.

Aging is associated with slowing of body functions, increased oxidative stress, reduced role of endogenous defense mechanisms. With age, reduced efficiency of thrombolysis, lower protection afforded by physical exercise against myocardial ischemia and more frequent manifestations of heart failure are more often observed.

It has not yet been established whether the patient’s older age or greater immune response to the virus or both are responsible for myocardial damage with subsequent complications

Direct viral infection, cytokine dysregulation and direct myocyte involvement can lead to acute myocardial injury in patients with COVID-19. Thus except for the high levels of CRP (C-reactive protein), elevated troponin levels suggest acute myocardial injury. It can be a result of myocarditis, ischemic injury, Takotsubo's cardiomyopathy, septic cardiomyopathy, acute cor pulmonale (as a result of acute pulmonary embolism).

Acute coronary syndromes can be a manifestation of imbalance between myocardial supply and demand as a result of systemic changes – hypoxemia, tachycardia, hypotension, vasoconstriction; or acute thrombosis in the coronary arteries. Often, when the right coronary artery is affected a complete atrioventricular heart block can be seen. Other location of the coronary lesion may lead to severe ischemic cardiomyopathy, left ventricular aneurysm formation with apical thrombosis.

The most frequent arrhythmia seen in COVID-19 patients is atrial fibrillation, which is a result of the acute respiratory failure. Electrolyte imbalance – hypokalemia and hypomagnesaemia can also lead to arrhythmic states.

Some of the medications used in the treatment of COVID-19 have proarrhythmogenic effects and should be used with caution, as they can provoke long QT interval, ventricular tachycardia and sudden cardiac death.

A hypercoagulable state and thrombotic events, that are related to markedly elevated D-dimer and fibrin degradation products, are thought to be secondary to systemic inflammatory response.

Takotsubo cardiomyopathy, predominantly seen in women, is mainly a result of increased sympathetic stimulation, which is usually observed in patients with COVID-19. It can be due to physical and psychological stress. This state can mimic acute coronary syndrome, which can develop within severe sepsis, hypoxemia, or metabolic acidosis.

Acute myocarditis due to myocardial inflammation can lead to ventricular dysfunction as a result of focal or global myocarditis or necrosis . Life- threatening arrhythmias can be a consequence of myocarditis. When linked with pericardial effusion, further deteriorating of the hemodynamics might lead to acute heart failure (HF) and cardiogenic shock .

The pathogenic mechanisms and clinical manifestations of cardiovascular complications of COVID-19 are presented in Table 2.

Cardiovascular disease	Pathogenic mechanism	Clinical manifestation
Acute coronary syndrome with or without ST elevation	Cytokine storm, hypercoagulability, plaque instability, imbalance between cardiac supply and demand	Typical chest pain or atypical pain and/or dyspnea, elevated levels of troponin, ECG changes (ST elevation or depression) and LV WMAs associated with specific region of distribution of a coronary

Cardiovascular disease	Pathogenic mechanism	Clinical manifestation
		artery
Myocarditis	Cytokine storm, direct cellular damage (possible)	Chest pain (possible), dyspnea (possible), elevated levels of troponin, ECG changes (possible), diffuse LV WMAs not related to specific coronary artery territory distribution
Pericarditis	Cytokine storm, direct cellular damage (possible)	Chest pain, dyspnea (possible), elevated troponin, ECG changes, impaired LV diastolic function and/or pericardial effusion
TTS	Emotional stress, microvascular and endothelial dysfunction, sepsis, acidosis, hypoxemia	Chest pain and/or dyspnea, elevated troponin, ECG changes, LV WMAs not related to specific coronary artery territory distribution (circumferential pattern, apical ballooning most frequently)
PE	Hypercoagulability	Chest pain and/or dyspnea, perioral cyanosis, elevated troponin (possible), ECG changes - S1Q3T3 pattern (possible), RV enlargement and dysfunction (McConnell sign, 60/60 sign)
Decompensated chronic HF	Hypoxia, elevated metabolic demand	Dyspnea, fatique, orthopea, tachydyspnea, hepatomegalia, anasarca, elevated levels of troponin (possible), LV WMAs without de novo abnormalities
Acute myocardial injury	Cytokine storm, direct cellular damage (possible), microvascular and endothelial dysfunction, hypoxia	Chest pain and/or dyspnea (possible), elevated levels of troponin, ECG changes (possible), LV WMAs (possible) not associated with specific coronary artery territory distribution (if

Cardiovascular disease	Pathogenic mechanism	Clinical manifestation
		absence of coexistent CAD)
Arrhytmias	Electrolyte abnormalities and medications for treatment of COVID 19 that have proarrhythmic effects	Dyspnea and chest pain (possible), ECG changes

Results. It has been established that symptoms of CVS damage in the post-COVID period are more common in patients with pre-existing pathology. Mechanisms that determine cardiovascular complications in PCS: viral invasion, dysregulation in the RAAS system, chronic inflammatory response, use of cardiotoxic drugs [1,3].

Pericarditis is more common with acute infection. However, in the observation of Silva Andrade B. and all. 7 patients developed pericarditis 20 days after clinical and virologic recovery from COVID-19 [1]. Other causes of pericarditis in the observation were excluded. It is hypothesized that post-covid pericarditis may be associated with ongoing inflammation maintained by the persistence of viral nucleic acid without viral replication in the pericardium.

Increased cytokine levels and respiratory distress syndrome also cause the progression of pre-existing left ventricular (LV) dysfunction or lead to the development of new cardiomyopathy [2]. One of the formidable CVS lesions in PCS is rhythm disturbance, which is most pronounced in patients with a severe course of the disease [3].

Conclusion. Considering that CVS lesions in post-COVID syndrome are more often observed in persons with pre-existing disorders, persons with chronic CVS diseases deserve special attention. Since CVD involvement in PCS can occur in even mild cases of COVID-19 survivors, knowledge of the manifestations of CVD involvement in PCS is important for developing treatment options for these patients.

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