

Altered cardiovascular health in COVID-19 patients

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Mortality due to cardiac cause is common amongst COVID-19 patients. Myocarditis, decompensated heart failure, acute coronary syndrome,¹ sinus tachycardia, atrial fibrillation and right bundle branch block (RBBB) were noted² in many hospitalized COVID patients. Studies conducted time to time, in various countries and hospitals registered various numbers and percentages (%) of patients suffering from myocardial injury ranging from 8% to 70% among the COVID victims.^{1,2,3} Infection by COVID-19 causes fever and inflammation in many organs and may cause serious myocarditis, even in those with no previous clinical history of cardiovascular disease.⁴ This infection may cause cardiomyopathy, altered rhythm, and reduction in optimum cardiac output.

As we know, the COVID-virus binds with angiotensin converting enzyme 2 (ACE2) expressed by the host cells and enters into the cell. The inner wall of cardiovascular system is laminated by endothelial cells. These cells also express ACE2 receptors. Damage of these cells by coronavirus causes inflammation within the vessels, results plaque rupture and heart attack.^{5,6} Furthermore, immune-inflammatory hyper-response and cytokine storm resulted by it may lead to inflammation-induced heart failure. Infected, inflamed, damaged endothelium induces activation of coagulation pathway.⁷ This may lead to deep vein thrombosis and acute pulmonary embolism in COVID-19 patients.^{8,9} Due to the compromised function of infected lungs and pulmonary thromboembolism, in COVID infected patients RBBB may develop. For hyper-coagulopathy and endothelial malfunction, compromised coronary flow may predispose myocardial ischemia, depicted as altered ST segment and T wave.

In COVID patients, the raised metabolic demand of inflamed cardiac tissue is not possible to satisfy by the oxygen supplied by the blood with existing PaO₂. This condition is termed as myocardial infarction type II.¹⁰ This challenging condition of heart further deteriorate by inadequate gas exchange in lungs, as lungs are also affected by coronavirus. So, in the heart with type II myocardial infarction, further reduction of oxygen supply by diseased lungs pushes it in worse condition.



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Severe coronavirus infection induces sympathetic over-activity, which may cause sinus tachycardia. It (sinus tachycardia) is a serious predictor of mortality.¹¹ Sympathetic stimulation induces profuse Ca^{++} entry into cardiac myocytes and spontaneous release of Ca^{++} ion from sarcoplasmic reticulum of cardio-myocytes resulting in arrhythmia.¹² Infection induces hyper-inflammatory response and thereby production of multiple cytokines like IL-1, IL-6, IL-8 etc. High titer of IL-6 is positively correlated with mortality.² IL-6 is cardio-toxic. Altered/increased IL-6 level decreases ICa^{2+} and L channel density and reduce transient intracellular Ca^{++} release. This impairs cardiac contractility and promotes supraventricular arrhythmia.^{13,14,15} Atrial fibrillations were noted in 10% ICU patients and had adverse prognosis.^{16,17} With normal K^+ level, atrial fibrillation occurs, may be due to hypoxia, acidosis or impaired balance of neuro-humoral or autonomic system. In severe COVID-19 infection, low number of CD+4 cells in periphery were noted and those were in exhausted state. Huge number of CD+4 T cells most probably entered myocardial tissue, caused inflammation, cytokine accumulation and resulted in atrial fibrillation.²

Besides IL-6, elevated troponin level was found to be a reliable marker among the COVID patients with cardiac problem. Highest mortality was noted in COVID patients with raised troponin and cardiovascular disease. Second highest mortality was noted in COVID patients with raised troponin and no previous clinical history of cardiovascular disease. Lesser mortality rate was registered in COVID patients with unraised troponin but with previous clinical history of cardiovascular disease. Lowest mortality rate was documented in COVID patients with unraised troponin and no previous clinical history of cardiovascular disease.¹⁸ Results also indicated that in COVID patients with elevated level of high sensitivity Troponin I, mortality rate was higher compared to those with normal level of the same [52% vs 45%].¹⁹

The virus interacts with angiotensin converting enzyme2 (ACE2) expressed by the host cells (cardio-myocytes, alveolar epithelium and other cells), enter into the cells and alter ACE2 signaling pathway.²⁰ ACE2, a carboxypeptidase, is cardio-protective; as it converts vasoconstrictor Angiotensin II to vasodilator angiotensin 1-7 (heptapeptides).²¹ Besides vasoconstriction, angiotensin II also acts as pro-inflammatory mediator and damages endothelium; so ultimately

fosters cardiovascular malfunction. COVID-19 virus causes down-regulation of ACE2.²² ACE2 can: (1) bind COVID virus and take it inside the cell, (2) convert angiotensin II to angiotensin 1-7, function of which is just opposite to angiotensin II. ie, cardio-protective. Experimental evidence established that renin angiotensin aldosterone system (RAAS) blockade by ACE inhibitors, ANG II type 1 receptor antagonists, mineralocorticoid antagonists, as well as statins, enhance ACE2. As patients with hypertension or other cardiovascular diseases are routinely treated with RAAS blockers and statins, new clinical concerns arose: Are these patients at greater risk for COVID infection? Should RAAS blockade and statin therapy be discontinued? However, cardiologists support the use of ACE inhibitors and/or angiotensin receptor blockers in COVID patients hospitalized with hypertension as co-morbidity as they experienced better survival rate with this treatment.²³

In short, raised IL-6 and troponin levels are reliable biomarkers of altered cardiovascular health in COVID-19 infected hospitalized patients indicating bad prognosis. Viral load must be minimized as quickly as possible. ACE inhibitors and angiotensin receptor blockers has to be continued in COVID affected cardiac patients.

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