ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 01 | January - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COVID-19 AND ACUTE CORONARY SYNDROMES (ACS): IMPLICATIONS OF RISK ASSESSMENT, DIAGNOSIS AND MANAGEMENT.

Cardiology

Noorush Shifa Nizami — Intern Clinosol Research, Doctor of Pharmacy, PHARM-D Clinosol research Private Limited, Ameerpet, Hyderabad, Telangana (500038), India. St Paul's College of pharmacy, Turkayamjal.

Dr. Ajit Singh* — Co-founder & Chief Executive officer, CliMed Research Solutions, Grugram, India-122001 National Director of Research, World Health Youth Federation, India *Corresponding Author

ABSTRACT

COVID-19, caused by SARS-COV-2, is creating devastation globally and is representing the greatest medicinal challenge in decades. In India, it is massive healthcare cause of interstitial pneumonitis and severe Acute Respiratory Distress Syndrome (ADRS).It also affects multiple organs and systems, particularly the cardiovascular system, of which most common cardiovascular complications include arrhythmia, cardiac injury, fulminant myocarditis, heart failure, pulmonary embolism, and Acute Coronary Syndrome (ACS). ACS in COVID-19 is attributed to demand-supply mismatch, whereas plaque destabilization may also contribute to it. The reports suggest that patients can present with chest pain and electrocardiographic changes suggestive of ACS with normal coronaries. This is a comprehensive review of the clinical course of COVID-19 with the cardiac comorbidities for future therapies.

KEYWORDS

Acute coronary syndromes, COVID-19, Acute myocardial infarction, Cardiovascular system.

INTRODUCTION:

The new coronavirus, first identified in the Chinese city of Wuhan, belongs to the family of viruses that includes the common cold and serious illnesses such as SARS (Severe Acute Respiratory Syndrome),and with time, it became a global emergency. Because of the spread, it is creating a massive healthcare problem. Patients with pre-existing cardiovascular diseases (CVD) having COVID-19 infection will be at higher risk of increased mortality and adverse outcomes that may ultimately lead to many cardiovascular complications. Andthe drugs used in the treatment of COVID-19 infection interact with cardiovascular drugs causing adverse cardiovascular effects[1,2,3]. If the infection becomes prevalent, the patients presenting the signs and symptoms of severe emergent CVD should be managed as COVID-19 suspects. SARS-COV-2 not only causes viral pneumonia but also has considerable implications for the cardiovascular system. Patients with cardiovascular risk factors including sex, advanced age, hypertension, obesity, diabetes, and also patients with the cardiovascularand cerebrovascular disease are identified as vulnerable populations with increased mortality and morbidity. In such populations, there is an increased risk of hospital stay apart from arterial and venous thrombotic complications presenting as ACS (acute coronary syndromes) and VTE (venous thromboembolism), and myocarditis.In patients with acute heart failure, these factors are reported to complicate the course of COVID-19 including the effects of medical treatment, owing to the redistribution of health care resources and access to emergency treatment including reperfusion therapy may be affected.

COVID-19 AND HEART FAILURE

Coronavirus is an enveloped, single-stranded ribonucleic acid (RNA) viruswith surface projectionscorresponding to the surface spike proteins. The transmission occurs by a combination of the spread of droplet and direct/ indirect contact, whereas the studies also suggest the transmission is possible through the air. The viral incubation period is 2 to 14 days. SARS-COV-2 enters cells to trigger an infection in ACE2, which is a multifunctional protein. Its physiological role is the enzymatic conversion of Angiotensin II to Angiotensin (1to7) and Angiotensin1 to Angiotensin (1 to 9), which are cardiovascular protective peptides, however in COVID-19 ACE 2 is also involved in SARS by its function as the coronavirus receptor. Also, binding of SARS-COV-2 spike proteins to ACE 2 facilitates viral entry into the lung's alveolar epithelial cells, where it will be highly expressed through the processes involving the cell surfaces associated with transmembrane protein serine 2 (figure 1). Within the host cell cytoplasm, and the viral genome i.e. RNA is released and starts replicating leading to newly formed genomic RNA, later processed into virion containing vesicles fused with the cell membrane to release the virus. SARS-COV-2 spreads mainly through the droplets, direct contact with an infected person, and respiratory secretions. The RAS/ACE 2 will be disrupted by the SARS-COV-2 infection[7].The infection likely plays a pathogenic role in respiratory failure and severe lung injury in COVID-19. Along with the lungs, ACE is highly expressed in the human heart, vessels, and gastrointestinal tract [8,9,10].

COVID-19 is a respiratory disease but many patients have underlying conditions. For example, CVD includes hypertension, Acute cardiac injury, and myocarditis which may be secondary to lung disease. Since acute lung injury itself leads to an increased cardiac workload and can present a problem especially in patients with pre-existing heart failure. Cardiovascular diseases may be a primary phenomenon considering the salient pathophysiological role of the RAS/ ACE -2 pathway in the cardiovascular system.

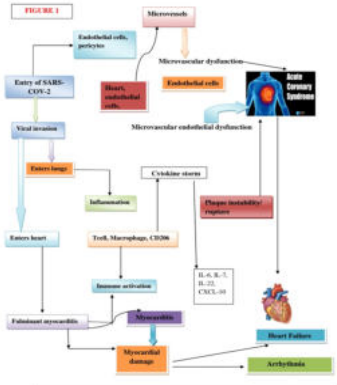

FIGURE 1 Cardiovascular involvement in COVID-19, its manifestations and hypothetical mechanisms. [10]

ACS (Acute coronary syndrome) in COVID-19 infection may be attributed to demand-supply mismatch and plaque destabilization. The altered hemodynamics and profound inflammatory response associated with the disease may cause the risk of atherosclerotic plaque rupture in susceptible patients [4]. It is crucial to note the potential overlapping symptoms between COVID-19 and ACS, while the predominant symptoms present in COVID-19 are respiratory reports showing electrocardiographic changes and chest pain/ chest discomfort are suggestive of ACS with normal coronaries. In patients presenting with ACS with un-ruled infection, isolation is preferred with hemodynamic monitoring until COVID-19 infection subsides.

The management of ACS patients should be determined by two factors

1. Risk stratification
2. Confirmed COVID-19/suspected COVID-19/ low-risk COVID-19 [5].

A conservative approach is recommended for all the ACS patients who are stable. Fibrinolysis is considered a reasonable option for stable STEMI patientspresenting within a stipulated time frame and without contraindications, as per standard protocols. However, invasive interventions may be limited to NSTEMI and STEMI with hemodynamic instability. Intervention should be done in the cardiac catheterization laboratory (CCL) only if proper personal protective equipment is available in an institute with a proper infection control unit. The CCL room should have negative pressure ventilation and if negative pressure is available, air conditioning i.e. laminar airflow and ventilation should be stopped. And all efforts should be made to perform a diagnostic test for COVID-19 before considering for PCI. Sick patients with definite or suspected COVID-19 are intubated before arrival to the catheterization laboratory to reduce aerosol exposure in the laboratory [6].

RISK OF COVID-19 IN PATIENTS WITH ACS

Cardiovascular diseases and cardiac risk factors are significant risk factors for COVID-19 and related complications[27]. A study shows a1% risk in theage group 50-59 years, 3% in those aged 60-69 years, 13% in aged 70-79 years, and 20% in the age group of 80 years and older. In China, patients with CVD had the highest case fatality rate i.e. 10% when compared to 7% with diabetes, 6% with a chronic obstructive pulmonary disorder, and 6% with hypertension, and lastly, 0% for those with no other comorbidities. Patients with a recent ACS may result in significant mortality[28].

Therefore, ACS/ Cardiac patients need to take extra care while following the standard precautions. The worsening of cardiovascular health is due to the combination of severe viral illness and increased demands on the heart. For example, fever causes a rapid heart rate. Compounded by the lower oxygen levels because of pneumonia and also the increase in propensity for blood formation. About 10% of the population with pre-existing cardiovascular disease (CVD) getting contracted will die, compared to 1% of the population who is healthy. An increased risk can also be seen in people with high blood pressure (Hypertension) and Coronary artery disease (CAD). Experts suggest that the missing link maybe because of the use of hypertension medications called angiotensin-converting enzyme (ACE)inhibitors and angiotensin-receptor blockers (ARBs) [38].

ACE inhibitors and ARB's may be useful as well as harmful. ACE and ARB's inhibitors are among the most commonly prescribed medications for the treatment of high blood pressure. And both the drugs have been proposed as a possible factor in the increased incidence of COVID-19 in people with high blood pressure and also heart problems[38].It is because of the observation that the coronavirus attaches to the ACE receptor, found in lung and heart tissue, and the spike proteins of coronavirus act like a key which locks into the epithelial cells that line the respiratory tract and to the air sac in the lungs, SARS-COV-2 will be undetected and the spike proteins will gain entry by unlocking the ACE 2 protein in the lung cells. After entering, they hijack the cell's mechanism and then replicate, multiply,and infect the adjoining cells[27].

People taking ACE inhibitors and ARBs produce anincreased number of receptors, which may increase the susceptibility of infection. On the contrary, ACE 2 has been found to protect against viral lung injury in mice. There is an ongoing study on Losartan, an ARB, that it may shieldpatients infected with COVID-19. Therefore, there is insufficient evidence of either benefit or harm. Also, there is a recommendation from The American College of Cardiology, American Heart Association, and Heart Failure Society of America that we should neither stop the use of ACE inhibitorsand ARBs in patients already taking them, nor prescribe them[38]. There are the different diagnostic approaches for ACS in COVID-19. (Table 1)

Table 1. Diagnosis of ACS in covid-19 infected population

1) CLINICAL PRESENTATION	A) Chest pain	Breathlessness and chest pain is a frequent symptom of COVID-19 infection. Chronic and acute coronary syndrome presentations can also be associated with respiratory symptoms[39].
	B) Dyspnea	Shortness of breath is one of the symptoms of COVID-19 [12].
	C) Cough	Cough is present in 59-81% of patients with COVID-19, most frequently unproductive cough [13,14].
	D) Acute respiratory distress	Characterized by bilateral opacifications on chest imaging and hypoxemia that cannot be explained by other causes[15]
	E) Cardiogenic shock	COVID-19 patients with impaired end-organ perfusion, at risk of cardiogenic shock-like large acute myocardial infarction, also considered as sepsis of possible or mixed etiology. Myocarditis should be considered as a precipitating cause. The key diagnostic testing in patients with cardiogenic shock includes ECG, bedside echocardiography, and emergent coronary angiography. Experimental evidence and clinical experiences indicate that more than 7.5% of myocardial cells have positive ACE 2 receptors expression [16].
	F) cardiac arrest, pulseless electric activity, sudden cardiac death, bradyarrhythmia, tachyarrhythmia.	The symptoms of bradyarrhythmia and tachyarrhythmias do not differ from the usual clinical presentation. In the SARS-COV-2 pandemic, health care professionals remain alert for symptoms of bradyarrhythmia or tachyarrhythmia[12].
	G) hospitalization due to pneumonia and increased subsequent risk of cardiovascular death	Pneumonia as well as influenza and SARS-COV-2 are well known to be associated with an increased short-term risk for subsequent cardiovascular events, such as ACS (Acute coronary syndromes). There should be high alertness for Cardiovascular events such as ACS and thromboembolic events. Fatal acute myocardial infections have been observed in the short term after COVID-19 associated SARS [17].
ELECTROCARDIOGRAM	Until now, no specific ECG changes have been described in patients with SARS-COV-2 infection. It is assumed that the overall minimal level of myocardial injury associated with the infection, as a consequence, the same ECG diagnostic criteria in cardiac condition apply in patients affected with SARS-COV-2 infection and also in the general population[18].	
BIOMARKERS ELEVATION SUGGESTING CARDIOVASCULAR CONDITIONS IN PATIENTS WIITH COVID-19 INFECTION:	A) Cardiac Troponin I/T	COVID-19 is viral pneumonia that results in severe systemic inflammation and ADRS and both conditions have profound effects on the cardiovascular system. The concentrations of cardiac troponin I/T in a patient affected with COVID-19 should be seen ina combination of the presence of pre-existing cardiac disease and acute injury related to COVID-19 infection [19].
	B) B – Type Natriuretic peptide/ N-Terminal B-type	This is a quantitative biomarker of hemodynamic myocardial stress and heart failure. Frequently elevated

	Natriuretic peptide	among patients with severe inflammatory or respiratory illness and seen as the combination of the presence of pre-existing cardiac disease/ acute hemodynamic stress related to COVID-19[19].
	C) D- Dimers	Generated by cleavage of fibrin monomers by prothrombin and indicate the presence of thrombin formation and indicates the presence of disseminated intravascular coagulation associated with shock and may contribute to myocardial injury. Hence recommended diagnostic algorithms can be used in case of suspected acute pulmonary embolism[20].
NON-INVASIVE IMAGING	Should not perform routine cardiac imaging in patients with suspected or confirmed COVID-19, prevent contamination from patients to other patients, to imaging equipment, a re-evaluation should be done in order to find which imaging technique is best for the patient both in terms of diagnostic yield and infectious risk for the environment[21].	
TRANSTHORACIC AND TRANSESOPHAGEAL ECHOCARDIOGRAPHY	Avoid performing transthoracic, transesophageal and stress echocardiograms in patients in which the results are unlikely to change the management strategy, Transesophageal echocardiography carries increased risks of spread of COVID-19 due to exposure of health care professionalto aerosolization of large viral load[22].	
COMPUTED TOMOGRAPHY	In patients with respiratory distress, lung CT is recommended to evaluate imaging features typical of COVID-19 and differentiate from other causes, heart failure, and pulmonary embolism. However, it should not be used to screen as a first-line test to diagnose COVID-19 and should be reserved for hospitalized patients[23].	
NUCLEAR CARDIOLOGY	Nuclear cardiology should be performed only in specific indications and when no other imaging modalities can be performed. Positron emission tomography (PET) minimizes the acquisition times[24].	
CARDIAC MAGNETIC RESONANCE	The role of CMR in COVID-19 patients is currently not clear. Accepted diagnostic indications for CMR should be considered appropriate in these patients, but should not be performed unless clinically necessary. CMR can be useful because in COVID-19 patients because the renal function will be decreased in COVID-19 patients and might contradict a clinically urgent CMR scan[25].	
EXERCISE TESTING	The performance of COVID-19 testing has major limitations in COVID-19. During the exercise, the patient increases breath rate and amount of aerosol production, and wearing the surgical mask could strongly affect his/her exercise capacity. Exercise testing is proposed as a method of choice for the diagnosis of heart failure with preserved ejection fractionin patients with breathlessness[26].	
DIFFERENTIAL DIAGNOSIS	Patients with COVID-19 infection can be presented with cardiac events, which include ACS (acute coronary syndromes), Acute heart failure, arrhythmias, thromboembolic events, cardiogenic shock, and cardiac arrests. These require quick diagnosis and management and should not be overlooked due to the presence of the COVID-19 infection.	
	Infection-related cardiac injury can lead to clinical presentation suggestive of a cardiac event and should also be considered as a differential diagnosis Patients with COVID-19 infection can be presented with clinical manifestations like Cardiovascular events, which include chest pain, dyspnea, shock, and even in the absence of cardiac injury[39].	

There is uncertainty whether the individual has an ACS due to plaque rupture. The combined use of clinical evaluation and ECG is usually sufficient for making a decision. Among the patients with COVID-19 and suspected ACS, the role of echocardiography to alter the probability of CAD is limited to low or intermediate-risk patients and in patients with COVID-19 infection, an echocardiogram may be performed. Findings of echocardiogram that relates to condition other than ACS (stress cardiomyopathy, myocarditis, pericarditis, or non-cardiac cause of chest pain) may include, absent wall motion abnormalities during the chest pain, wall motion abnormalities which do not support regional injury suggested by ECG, wall motion abnormalities in the non-coronary distribution, less specific findings, including small pericardial effusion.

Cardiogenic shock is the primary disorder in the majority of patients with severe COVID-19 in hypoxia-related respiratory failure. This develops systemic hyper-inflammatory response and vasodilatory shock as viremia clears, this phase may be accompanied by concomitant cardiogenic shock and myocardial suppression. This mixed etiology may be difficult to manage, if the patient has pre-existing cardiovascular dysfunction, and it has been observed that severe cardiovascular dysfunction occurs with mild respiratory inflammation[40].

MANAGEMENT OF COVID-19 ASSOCIATED WITH MYOCARDIAL INJURY.

The management of patients with non-ST segment elevation should be done by risk stratification, and the testing for COVID-19 should be performed at earliest and the patients should be categorized into 4 groups. (Figure 2 represents the recommendations for the management of patients with NSTE-ACS in COVID-19 outbreak)[30].

There is limited data obtained from high-quality studies for the pharmacotherapy of myocardial injury associated with COVID-19. And the treatment should be completed with a multidisciplinary team that may include infectious diseases consultation to help guide therapy selection.

- Hydroxychloroquine is the proposed treatment for COVID-19 based on in-vitro testing with methodological limitations[30].
- Antiviral therapies may be beneficial in treating acute coronary syndromes. The use of Ritonavir/Lopinavir for severe COVID-19 was studied prospectively in 199 patients but there was no significant reduction in symptomatic improvement and reduction of viral load[31]. And most importantly, in-vitro testing of the human cell line demonstrated reduced SARS-COV-2 activity, because of which there is compassionate use of remdesivir in patients with COVID-19. Both Hydroxychloroquine and antiviral therapy will eventually increase the risk of torsades de points through the prolongation of QTc [32].
- Immunosuppression for myocardial injury in COVID-19 has been a proposed treatment option. In the treatment of myocarditis, no significant difference was seen in the left ventricular ejection fraction between patients who are being treated with cyclosporine or prednisone, those who are being treated with azathioprine or prednisone, and those patients who are receiving placebo among the patients with myocarditis in the pre-COVID-Era; this investigation concluded that glucocorticoid therapy did not reduce the composite endpoint of heart transplantation[33]. There were certain limitations of the trial so the resultsdo not support the widespread use of immunosuppressive therapies for myocarditis. A systemic review evaluated the efficiency of the steroids in acute viral myocarditis and this investigation concluded that glucocorticoid therapy will not reduce the composite endpoint of heart transplantation, hence steroids may prolong SARS-COV-2 viral persistence, so corticosteroid treatment should not be routine but rather it can be considered as salvage therapy [34].
- Cytokine activation is a prominent feature of severe COVID-19

with elevations of interleukin-6 and other inflammatory markers. Siltuximab, sarilumab, and tocilizumab are interleukin-6 inhibitors that have potential utility in COVID-19[34].

- The association between myocarditis and autoantibodies, immunoglobulins intravenously is theorized as the possible treatment for virus-associated myocarditis, and it is important to note that this is an extremely limited resource and should be reserved for the patients with an increased clinical suspension of cardiomyopathy resulting from myocarditis rather than cytokine storm or stress-induced cardiomyopathy[35].
- Antibody therapy using convalescent plasma from the recovered patients with COVID-19 has also been approved by the US Food and Drug Administration. And the recent study described the treatment of 5 critically ill patients with convalescent plasma containing the SARS-COV-2 specific antibody which was obtained from survivors of COVID-19[36].
- If the patient recovers from COVID-19 and myocardial injury is diagnosed clinically, similar to the historical expert opinion recommendations for the Non-COVID myocarditis abstinence from aerobic activity would be reasonable for a period of 3 to 6 months until the resolution of myocardial inflammation by cardiac magnetic resonance imaging [37].
- In cases with refractory shock/ ventricular arrhythmias caused by cardiovascular syndrome/myocardial injury, mechanical support could be considered. Case reports have described the successful rescue of the patients with cardiogenic shock by using the veno-arterial and veno-arterial-venoextracorporeal membrane oxygenation[11,37]. (Figure-2)

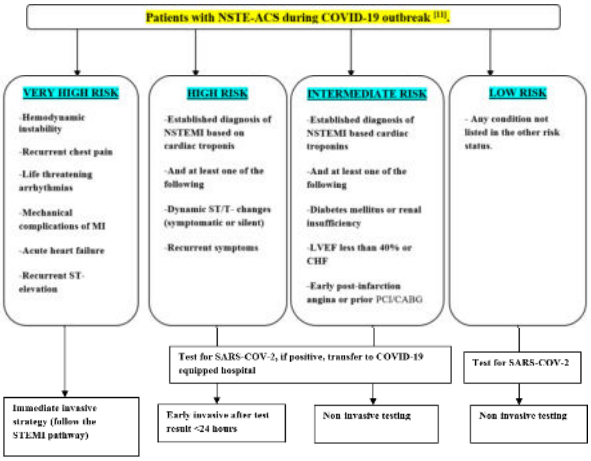

Figure 2 Risk Stratification and testing strategy for ACS in COVID-19

LOW AND INTERMEDIATE-RISK NSTEMI

Patients with low- and intermediate-risk NSTEMI do not need immediate revascularization. COVID-19 patients should be performed with the same modalities before their transfer to the laboratory/ their admittance to the cardiology ward. While waiting for COVID-19 results a proper risk assessment should be carried out and soon after the test results patients with NSTEMI and positive COVID-19 test should be admitted to isolation units within the appropriate care settings depending on the thrombotic and arrhythmic risk and clinical condition, evaluating the risk-benefit ratio from possible revascularization[41]

FACTORS THAT REQUIRE SPECIAL ATTENTION FOR ACS MANAGEMENT DURING COVID-19 PANDEMIC[29].

- Training of the medical and paramedical staff about early recognition of COVID-19 infection, measures of disinfection for medical equipment, and training of PPE use is mandatory.
- Acute myocarditis and myocardial injury due to COVID-19 infection can pretend ACS. Increased troponin results are very common, especially in high sensitivity cardiac troponin assays. So increased troponin values may not be helpful in the diagnosis of ACS during COVID-19 infection.
- Rapid detection methods can reduce the time delay and may be helpful for quick triage of COVID-19 test result in ACS.
- Patients can be diagnosedwith the infection during the course of hospital stay, hence regular assessment of risk-benefit ratio for ongoing medical treatment is mandatory.
- In every city, at least a few of the CCUs (coronary care units) should be established in hospitals for COVID-19 patients.
- Delayed presenters of STEMI will significantly increase. This is due to lack of proper transport, reluctance to attend hospital in present conditions, and also fear of getting the infection from the health care system.
- Coagulation parameters will be deranged during severe COVID infection, which needs to be considered before giving antiplatelets and close monitoring of bleeding parameters is required in such situations.
- Drugs that are used in the treatment of COVID-19 such as Anti-viral drugs should be selected wisely. For example, Ribavirin has no direct toxicity over the cardiovascular system and Lopinavir/Ritonavirmay result in PR and QT interval prolongation, mainly in patients with baseline abnormality i.e. long QT or those who are at risk for conduction abnormalities including those taking other QT prolongation drugs.
- Dosing of Anticoagulant drugs: Ribavirin has variable effects on warfarin dosing, ritonavir/lopinavir may need dose reductions or neglecting CYP3A4 mediated drugs such as Apixaban and rivaroxaban. Through the CYP3A4 inhibition, Lopinavir/ Ritonavir causes increased serum concentrations of ticagrelor, therefore the concomitant use of ticagrelor should be discouraged due to heavy bleeding risk as per reports by USA and Canada. Clopidogrel may not provide sufficient platelet inhibition during concomitant administration of Ritonavir/Lopinavir but it was not the same with Prasugrel. If Prasugrel cannot be used, testing a guided approach with platelet function assays is strongly recommended.
- Co-administration of Ritonavir/Lopinavir with statins may result in myopathy due to elevated statin levels. Simvastatin and Lovastatin are contraindicated for co-administration with Ritonavir/ Lopinavir for the risk of rhabdomyolysis, Rosuvastatin should be administered at the lowest possible dose.
- Hydroxychloroquine is a QT prolonger, hence, cautious use should be done in ACS patients and the same for Azithromycin and its combination with Hydroxychloroquine. Careful use with a more frequent assessment of QT intervals is needed for Antiarrhythmic drugs, known to cause QT prolongation, especially Amiodarone.
- ACE/ARB (Angiotensin converting enzymeinhibitor/ Angiotensin Receptor Blocker) is usually used in the post ACS setting. It is recommended to continue the use of ACEI/ARB in the treatment of hypertension, heart failure, post-myocardial infarction, and other conditions during COVID-19.
- Follow up with the telehealthcare systems should be extended for stable patients to minimize the hospital visits. All the medical practitioners are encouraged to be familiar with the updated guidelines through online programsmade available by the board of governors of MCI.

CONCLUSION:

COVID-19 pandemic is creating a global public health burden, with a progressively increasing number of infected subjects, which are generally asymptomatic, in this emergency crisis. Cardiologists can improve their approaches in the management of acute coronary syndromes (ACS), not just to guarantee the appropriate treatment to ACS patients, also by following proper guidelines, they may protect the hospital environment from the virus spread. Because of the COVID-19 pandemic, the cardiovascular emergency is exposed to the balancing timelines of the treatment and also the safety of health care professionals and other patients. Each patient referred to the outpatient department and cath lab requires exclusion of COVID-19 infection. For the confirmed cases specific measures should be undertaken which are mentioned such as factors that require special attention for ACS management during COVID-19 pandemic and high protection level of health care professionals.

This document provides a short and simple guide to assist clinicians in the implications of risk assessment, diagnosis, and management of ACS considering COVID-19 and protecting the high-risk cardiac patients during the COVID-19 outbreak.

REFERENCES:

1} Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin RES cardiol. 2020. Available at https://doi.org/10.1007/s00392-020-01626-9.2.
2} Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system.NatRev Cardiol. 2020 Mar 5.available at https://doi.org/10.1038/s41569-020-0360-5.3.

3} Driggin Elissa, Madhavan Mahesh M, Bikdeli Behnood, et al. Cardiovascularconsiderations for patients, health care workers, and health systems during thecoronavirus disease 2019 (COVID-19) pandemic.JACC (J Am Coll Cardiol). 2020. Available at https://doi.org/10.1016/j.jacc.2020.03.031.
4} Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adultinpatients with COVID-19 in Wuhan, China: a retrospective cohort study.Lancet. 2020 March 28;395(10229):1054e1062. Available at https://doi.org/10.1016/S0140-6736(20)30566-3
5} Jing Zhi-Cheng, Zhu Hua-Dong, Yan Xiao-Wai, Chai Wen-Zhao, Zhang Shuyang,COVID-19&AMI Committee of Peking Union Medical College Hospital. Rec-ommendations from the Peking Union Medical College Hospital for the management of Acute Myocardial Infarction during the COVID-19 outbreak.EurHeart J. 2020 March 31. Available at https://doi.org/10.1093/eurheartj/ehaa258
6} Santanu Guha, Somnath Mukhopadhay, et al. Managing ACS during COVID-19 infection: do not follow traditional route, India. 2020 April. , Indian heart journal 72 (2020) 128-130. Available at https://www.sciencedirect.com/science/article/pii/S0019483220300602
7} Wu Y. Compensation of ACE 2 function for possible clinical management of 2019-n-COV-induced acute lung injury. Virol sin 2020. Available at https://doi.org/10.1007/s12250-020-00205-6
8} Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 2004;203(2):631-7. Available athttps://doi.org/10.1002/path.1570
9} Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020;14(2):185-192. Available athttps://doi.org/10.1007/s11684-020-0754-0
10} Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, Madhur MS, Tomaszewski M, Maffia P, D'Acquisto F, Nicklin SA, Marian AJ, Nosalski R, Murray EC, Guzik B, Berry C, Touyz RM, Kreutz R, Wang DW, Bhella D, Sagliocco O, Crea F, Thomson EC, McInnes IB. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res 2020 available at. https://doi.org/10.1093/cvr/cvaa106
11} Andreini, Daniele . et al. ECS (European society of cardiology) guidance for the diagnosis and management of CVD during the COVID-19 pandemic . Available athttps://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance
12} Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS, China Medical Treatment Expert Group for C. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382(18):1708-1720. Available athttps://doi.org/10.1056/NEJMoa2002032
13} Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054-1062. Available at https://doi.org/10.1016/S0140-6736(20)30566-3
14} Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F, Jiang J, Bai C, Zheng J, Song Y. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020. Available athttps://doi.org/10.1001/jamainternmed.2020.0994
15} Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R, Brochard L, Brower R, Esteban A, Gattinoni L, Rhodes A, Slutsky AS, Vincent JL, Rubenfeld GD, Thompson BT, Ranieri VM. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med 2012;38(10):1573-82. Available athttps://doi.org/10.1007/s00134-012-2682-1
16} Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front Med 2020;14(2):185-192. Available athttps://doi.org/10.1007/s11684-020-0754-0
17} Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL, Law KI, Tang BS, Hon TY, Chan CS, Chan KH, Ng JS, Zheng BJ, Ng WL, Lai RW, Guan Y, Yuen KY, Group HUSS. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet 2003;361(9371):1767-72. Available athttps://doi.org/10.1016/s0140-6736(03)13412-5
18} Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, Cani DS, Cerini M, Farina D, Gavazzi E, Maroldi R, Adamo M, Ammirati E, Sinagra G, Lombardi CM, Metra M. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol 2020. Available athttps://doi.org/10.1001/jamacardio.2020.1096
19} Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B, Huang C. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol 2020. Available athttps://doi.org/10.1001/jamacardio.2020.0950
20} Giannitsis E, Mair J, Christersson C, Siegbahn A, Huber K, Jaffe AS, Peacock WF, Plebani M, Thygesen K, Mockel M, Mueller C, Lindahl B, Biomarker Study Group of the European Society of Cardiology Acute Cardiovascular Care A. How to use D-dimer in acute cardiovascular care. Eur Heart J Acute Cardiovasc Care 2017;6(1):69-80. Available athttps://doi.org/10.1177/2048872615610870
21} Gluckman TJ. General guidance on deferring non-urgent cv testing and procedures during the COVID-19 pandemic.
22} Soldati G, Smargiassi A, Inchingolo R, Buonsenso D, Perrone T, Briganti DF, Perlini S, Torri E, Mariani A, Mossolani EE, Tursi F, Mento F, Demi L. Is There a Role for Lung Ultrasound During the COVID-19 Pandemic? J Ultrasound Med 2020.Available athttps://doi.org/10.1002/jum.15284
23} Choi AD, Abbara S, Branch KR, Feuchtner GM, Ghoshhajra B, Nieman K, Pontone G, Villines TC, Williams MC, Blankstein R. Society of Cardiovascular Computed Tomography guidance for use of cardiac computed tomography amidst the COVID-19 pandemic Endorsed by the American College of Cardiology. J Cardiovasc Comput Tomogr 2020. Available athttps://doi.org/10.1016/j.jcct.2020.03.002
24} Skali H, Murthy VL, Al-Mallah MH, Bateman TM, Beanlands R, Better N, Calnon DA, Dilsizian V, Gimelli A, Pagnanelli R, Polk DM, Soman P, Thompson RC, Einstein AJ, Dorbala S. Guidance and Best Practices for Nuclear Cardiology Laboratories during the Coronavirus Disease 2019 (COVID-19) Pandemic: An Information Statement from ASNC and SNMMI. Zenodo 2020. Available at https://doi.org/10.5281/zenodo.3738020
25} Society for Cardiovascular Magnetic Resonance. SCMR's covid-19 preparedness toolkit. https://scmr.org/page/COVID19
26} Pieske B, Tschope C, de Boer RA, Fraser AG, Anker SD, Donal E, Edelmann F, Fu M, Guazzi M, Lam CSP, Lancellotti P, Melenovsky V, Morris DA, Nagel E, Pieske-Kraigher E, Ponikowski P, Solomon SD, Vasan RS, Rutten FH, Voors AA, Ruschitzka F, Paulus WJ, Seferovic P, Filippatos G. How to diagnose heart failure with preserved ejection fraction: the HFA-PEFF diagnostic algorithm: a consensus recommendation from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur Heart J 2019;40(40):3297-3317.Available athttps://doi.org/10.1093/eurheartj/ehz641
27} Noorush Shifa Nizami, CS mujeeb uddin. Strong immunity- A major weapon to fight against COVID-19. IOSR Journal of pharmacy and Biological sciences. E-ISSN:2278-3008, p-ISSN: 2319-7676. Volume 15, Issue 3 ser.III (may-june 2020) ,PP 22-29. Available at http://www.iosrjournals.org/iosr-jpbs/pages/15(3)Series-3.html
28} Sean Coffey, Anouska Moynagh et al. Changes to management of a non-pandemic illness during the COVID-19 pandemic: case study of invasivemmanagement of Acute coronary syndrome, open access. New Zealand medical journal, vol 133 no 1513, 24th april 2020. Available at https://scholar.google.com/scholar?start=10&q=covid+and+management+of+ACS&hl=en&as_sdt=0,5#d=gs_qabs&u=%23p%3DA8DNmzkk0o8J
29} Santanu Guha, Rakesh yadav, et al. Managing ACS during COVID-19 infection: do not follow traditional route, India. 2020 April. , Indian heart journal 72 (2020) 128-130. Available at https://www.sciencedirect.com/science/article/pii/S0019483220300602
30} Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, Doudier B, Courjon J, Giordanengo V, Vieira VE, et al.. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial [published online March 20, 2020].Int JAntimicrob Agents. doi: 10.1016/j.ijantimicag.2020.105949. Available at Google scholar
31} Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, Ruan L, Song B, Cai Y, Wei M, et al.. A trial of lopinavir-ritonavir in adults hospitalized with severe COVID-19.N Engl J Med. 2020; 382:1787–1799. doi:10.1056/NEJMoa2001282. Available at CrossrefMedline Google Scholar
32} Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao G. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro.Cell Res. 2020; 30:269–271. doi: 10.1038/s41422-020-0282-0. Available at CrossrefMedlineGoogle Scholar
33} hen HS, Wang W, Wu SN, Liu JP. Corticosteroids for viral myocarditis.Cochrane Database Syst Rev. 2013:CD004471. doi: 10.1002/14651858.CD004471.pub3. Available at MedlineGoogle Scholar
34} Ascierto PA, Fox B, Urba W, Anderson AC, Atkins M, Borden EC, Brahmer JR, Butterfield LH, Cesano A, Chen DS, et al.. Insights from immuno-oncology: the Society for Immunotherapy of Cancer statement on access to IL-6-targeting therapies for COVID-19.J Immunother Cancer. 2020; 8:e000878. doi: 10.1136/jitc-2020-000878. Available at CrossrefMedlineGoogle Scholar
35} US Food and Drug Administration. Recommendations for investigational COVID-19 convalescent plasma.April 13, 2020. Available at https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/investigational-covid-19-convalescent-plasma-emergency-inds.
36} Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, Wang F, Li D, Yang M, Xing L, et al.. Treatment of 5 critically ill patients with COVID-19 With convalescent plasma.JAMA. 2020; 323:1582–1589. doi:10.1001/jama.2020.4783. Available at https://jamanetwork.com/journals/jama/fullarticle/2763983
37} Zeng JH, Liu XY, Yuan J, Wang F, Wu W, Li J, Wang L, Gao H, Wang Y, Dong C, et al.. First case of COVID-19 complicated with fulminant myocarditis complication: case report and insights [published online March 11, 2020].Infection. doi: 10.20944/preprints202003.0180.v1. Available at Google Scholar
38} Dara K. Lee Lewis, MD. How does cardiovascular disease increase the risk of severe illness and death from COVID-19 illness. Harvard health publishing april, 2020. Harvard health blog. Available at https://www.health.harvard.edu/blog/how-does-cardiovascular-disease-increase-the-risk-of-severe-illness-and-death-from-covid-19-2020040219401
39} ESC Guidance for diagnosis and management of CV Disease during the COVID-19 pandemic. Updated on 10 june 2020. Available at https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance.
40} Duane S pinto, MD, MPH. Coronavirus disease 2019 (COVID-19); Myocardial infraction and other coronary artery disease issues. June 2020. Available at https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-myocardial-infarction-and-other-coronary-artery-disease-issues#H2004091134
41} Bernard Katz Legacy. Acute Coronary Syndromes During COVID-19- A simple short guide from Italy to assist in the management of ACS during the COVID-19 pandemic is presented. Available at https://academic.oup.com/eurheartj/article/41/22/2047/5843749