Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Review article

A review of cardiac manifestations and predictors of outcome in patients with COVID – 19

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ABSTRACT

Coronavirus disease (COVID-19) pandemic has so far involved 184 countries and more than 2.79 million patients worldwide. Over the past three months, it has attributed to more than 196,000 deaths, with more than 50,000 deaths in the United States alone. Pulmonary manifestations are predominant and have been well identified. Cardiac involvement is also common. Acute cardiac injury, the most common cardiac manifestation of this disease can be seen in patients even without prior cardiac comorbidities. Established cardiovascular risk factors such as diabetes mellitus, hypertension, and coronary artery disease predispose to cardiac injury, the severity of illness and mortality. Non-ischemic myocardial injury secondary to cytokine storm is thought to be the predominant mechanism of acute cardiac injury associated with COVID-19. Multiple mechanisms and processes contribute to cardiac injury resulting in a poor outcome. Some of these are not clearly understood. Clinical and diagnostic details of cardiovascular involvement in these patients are mostly limited to biochemical markers. Multiple therapeutic agents have been tried with questionable efficacy and without clinical evidence. Interactions of comorbidities, cardiovascular drugs, the cardiac effect of therapeutic agents on the illness continue to be under investigation. With an increasing number of patients, newer promising therapies, and ongoing clinical trials, the exact mechanisms and extent to which these risk factors contribute to outcomes will be clearer in the future.

Introduction

Starting from the initial clusters of cases in December 2019 to date; presentation, knowledge, and implications of novel coronavirus infection have changed significantly. With an ongoing spread worldwide and increasing mortality, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is now a pandemic and public health emergency of international concern as per the World Health Organization.[1] As of April 24th, the total number of reported cases of COVID-19 globally has been 2.79 million of which 923,000 have been in the United States. The clinical presentation of this disease is mostly pulmonary, with computed tomography of chest contributing to the diagnosis and facilitating the staging and severity of the disease.[2,3] Reports of cardiac manifestations of COVID-19 infection are on the rise.[4,5] In this review, we discuss the various cardiovascular manifestations of this disease. We have aimed to discuss in detail the pathophysiology, cardiovascular manifestations of the infection, and a concise review of articles published with data from the present pandemic.

Epidemiology

Cardiovascular involvement has been uniformly reported in patients with COVID 19. New cardiovascular manifestations mostly reported as an acute myocardial injury is seen in less than 10% of patients.[6,7] Cardiovascular comorbidities including hypertension, diabetes mellitus (DM), coronary artery disease, heart failure have been reported in larger numbers. The largest study including 72,314 patients reported a higher case fatality rate in patients with prior cardiovascular comorbidities including coronary artery disease (10.5%), DM (7.3%), and hypertension (6%).[8] With an increasing number of cases and reports on clinical outcome, further update on literature with regards to cardiac manifestations and its outcome can be expected.

Pathophysiology

SARS-CoV-2 uses membrane-bound angiotensin-converting enzyme 2 (ACE 2) to enter target cells.[7,9] ACE 2 is highly expressed in the oral cavity and tongue facilitating viral entry. ACE 2 is also expressed in alveolar epithelial cell type I, II in the lung resulting in the predominant pulmonary manifestations. Similarly, higher ACE 2 gene expression has been reported in patients of East Asian ethnicity

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and smokers. Whether that makes them more susceptible is yet unknown.[10–13] In the heart, ACE 2 is predominantly located in cardiac endothelium, cardiac myocytes, and smooth muscle cells of the myocardial vessels. Even though ACE 2 is highly expressed in the heart, the exact mechanism of cardiac injury is not yet completely understood.[14]

Two distinct processes of acute cardiac injury that have been discussed so far in COVID-19 are non-ischemic myocardial injury and myocardial ischemia.[6,15,16] Among these, non-ischemic myocardial injury has been reported predominantly across most studies. Multiple distinct mechanisms for non-ischemic myocardial injuries that have been published in the literature include– [i] cytokine storm, as documented by significantly elevated inflammatory markers like C- reactive protein, ferritin, procalcitonin, etc, [ii] secondary to hemophagocytic lymphohistiocytosis following infection, [iii] viral myocarditis with reports of progression to fulminant myocarditis, [iv] stress cardiomyopathy, and [v] hypoxia- induced cardiac myocyte apoptosis.[6,14,17]

Ischemic injury though postulated, has not been supported by evidence yet. Systemic inflammation, inflammation- induced prothrombotic state and increased shear stress following increased coronary blood flow has been postulated to precipitate plaque rupture causing features of acute coronary syndrome.[6,14]

Other cardiovascular mechanisms that have also been thought to cause poor outcomes are dyselectrolytemia (such as hypokalemia) and cardiac medications acting on the Renin – Angiotensin- Aldosterone axis (such as angiotensin receptor blockers), other drugs including statins,various antiviral agents, steroids, hydroxychloroquine, and azithromycin.[6,18,19] However, these reports are anecdotal and lack a robust basic-science basis to be used as clinical evidence at present. Fig. 1 represents the 3 principal factors contributing to cardiac injury in patients with COVID – 19. Older patients can have multiple contributors to cardiac injury as shown in the image, predisposing them to a higher risk of the poorer outcome.

Cardiac enzymes including high sensitive troponin I (cTnI) are elevated in all the above-mentioned processes following cardiac injury irrespective of the mechanism.[4] Also elevated troponin I levels have been uniformly associated with disease severity among patients with inflammation secondary to cytokine storm.[17,20,21] Uncontrolled, continuous, dysfunctional activation of the immune system resulting in excessive cytokine release has been shown with findings of elevated plasma levels of Interleukins (IL-2, IL-7), granulocyte – colony stimulating factor, IgG- induced protein 10, chemokine ligand 3 and tumor necrosis factor alpha among patients admitted to intensive care units with COVID-19. Patients with cardiac injury also have been reported to have higher plasma inflammatory markers levels of procalcitonin, ferritin, D- dimer, C- reactive protein (CRP) and leukocytes.[7,17,21] Among these an elevated cTnI, and an up- trending cTnI is instrumental in the diagnosis and predicting outcome in patients with cytokine storm related cardiac injury. In multiple studies, this cytokine storm related cardiac injury has also been reported to predict outcomes including acute respiratory distress syndrome (ARDS), acute kidney injury, the severity of illness, requirement of intensive care unit admission and mortality.[14,15,17,22]

Cardiac manifestation

Pericardium

Pericardial effusion has been reported in patients. The study including 90 patients who underwent non contrast computed tomography (CT) of chest reported pericardial effusion in 1% of patients.[23] In this study, the authors also reported that in more than 70% of patients there was evidence of disease progression on the subsequent CT. However, Wu et al in their study did not find this trend or appearance of a new pericardial effusion at follow up imaging done within 6 days.[22] Another study reported around 4–5% of patients with pericardial effusion. In this study Li et al reported that the presence of pericardial effusion was significantly higher among patients with severe disease, indicating the presence of significantly higher inflammation.[3,24]. The same has been demonstrated in autopsy showing pericarditis in patients.[25] There are isolated case reports of pericardial effusion being documented on echocardiography of COVID-19 patients. [26] Table 1 summerizes the pericardial findings in patients with COVID-19.

Myocardium

Myocardial involvement mostly presents as an acute cardiac injury in around 8–12% of patients. This has been defined by elevated serum cardiac biomarkers, presence of new rhythm abnormalities in the electrocardiogram, or abnormal finding in the echocardiogram of an infected patient.[6,14,17] Transient, reversible left ventricular dysfunction, and cardiogenic shock have also been reported. In patients with viral myocarditis, recovery of cardiac structure and function is noted. Only mononuclear infiltrates have been reported in the myocardial tissue autopsy in the setting of high viral load. There have

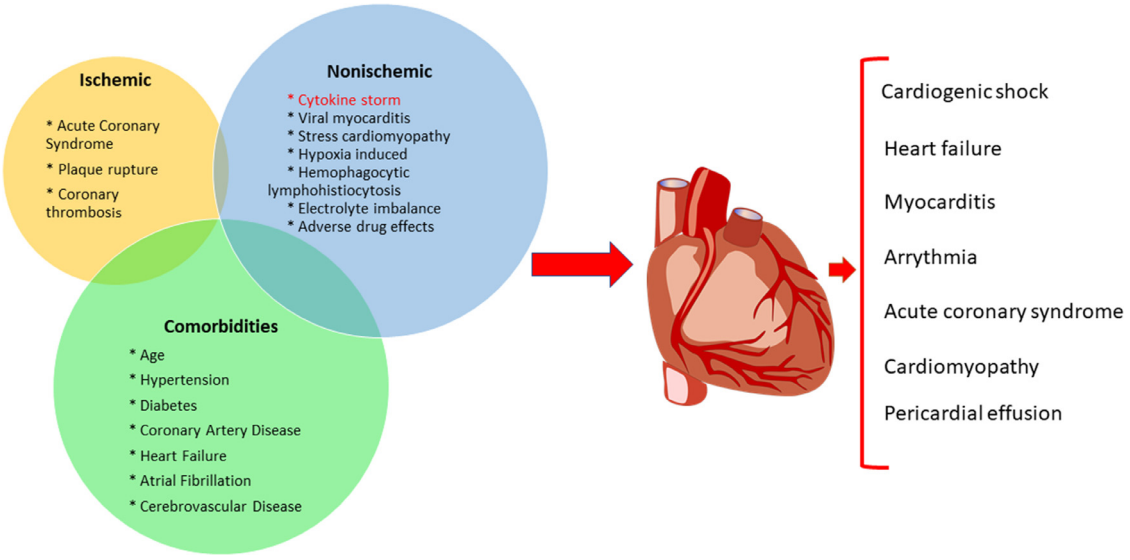

Fig. 1. Mechanism and patterns of cardiac injury in COVID-19

Table 1
Summary of pericardial findings from prior studies

	wu et al(2)	Xu et al(4)	Li et al(5)
Modality of imaging	CT Chest	CT Chest	CT Chest
Total patients	80	90	83
Pericardial effusion	4 (5%)	1 (1%)	4 (4.8%)
Predictor of outcome	–	–	+

been reports of fulminant myocarditis with elevated troponin and improvement in left ventricular function following intravenous immunoglobulin and steroids, and subsequent normalization of troponins .[26,27]

Other structures

Reports describing the involvement of endocardium, valves, supporting structures, vascular territories secondary to the infection have not been published in literature as yet. Among the patients with fulminant myocarditis, with left ventricular dilatation, and acute reduction in ejection fraction, a new onset valvular dysfunction has not been found. Evidence of pulmonary artery hypertension has been reported in some patients.[5] Even though there are reports of increased cardiac arrhythmia in patients, direct viral invasion and involvement of the conduction system has not been confirmed.[6,7,15]

Clinical presentation

Fever and cough continue to be the most common presenting symptoms of patients with COVID-19. Respiratory symptoms predominate the clinical picture. Symptoms of shortness of breath, fatigue, palpitations, chest pain, have been reported in 28%, 13%, 7.3%, and 3.4% of patients respectively.[6,14,21] A small retrospective study has reported that the presence of chest pain correlated with significant myocardial injury.[21]

Physical examination

Similarly, there is limited data on cardiac examination findings. Tachycardia and high blood pressure have been reported in patients, with the latter being linked to a poor outcome. Among the patients who had presented with pericardial effusion and myocarditis, no significant cardiac findings were reported on physical examination. The above could be because of the prominence of respiratory findings, technical difficulties in the assessment of patients on mechanical ventilation, and limited scope of the systemic cardiac examination.

Diagnosis

Cardiac involvement in most studies has been based on elevated cardiac biomarkers. High-sensitivity troponin level has been consistently reported in patients with cardiac involvement.[4,7,8] Details of electrocardiography and echocardiography has not been uniformly reported in most studies. Even though details of multiple cardiac and inflammatory markers are available, these have been used as associative markers.[21,28]

Electrocardiography

Data on EKG findings on patients with COVID-19 is scanty. In a study including 416 hospitalized patients only 82 (19.7%) patients were thought to have a cardiac injury. Among those who had cardiac injury only 27% of people underwent an EKG. Among these 63% of EKGs were done correlating with elevated cardiac enzymes. These EKGs showed non-specific findings of cardiac injury including T wave depression and inversion, ST segment depressions, and presence of Q waves.[21] Other significant EKG changes have been ST segment elevation of leads III and AVF and sinus tachycardia.[14,17] We had recently seen a patient with heart failure and reduced ejection fraction presenting with EKG evidence of new onset atrial fibrillation and rapid ventricular rate.

Biochemical markers

Biochemical markers including elevated lactate dehydrogenase (LDH), creatinine kinase (CPK), creatinine kinase MB (CK-MB), D – dimer, high-sensitivity troponin has been reported to be elevated in patients with COVID -19 related cardiac injury.[15,17,21] Patients with elevated LDH, CK - MB, and D - dimer have been reported to be at a significantly higher risk for requiring ICU care. High-sensitive troponin has been consistently used across all studies to report cardiac injury. Acute cardiac injury has been defined as an elevated high-sensitive troponin level above the 99th percentile of upper reference limit in the studies reporting the same.[4,8,17,20]

Chest X- ray

Most chest x- rays have prominent pulmonary parenchymal features and non significant cardiac findings. However, in a 37-year-old man presenting with coronavirus fulminant myocarditis, an initial chest x-ray showed findings suggestive of cardiomegaly. Interestingly one week later, at the time of discharge repeat chest x-ray showed normalization of cardiac silhouette.[26]

Echocardiography

In most studies, the number of patients undergoing echocardiography is scanty. Reported studies have described findings in transthoracic echocardiograms in patients with suspected cardiogenic shock. Reported abnormalities in patients with evidence of fulminant COVID-19 myocarditis include diffuse myocardial dyskinesia, left ventricular enlargement, reduced left ventricular ejection fraction, pulmonary hypertension, reduced IVC collapsibility, and pericardial effusion.[17,26,27] Reports have also shown normalization of left ventricular diameter, wall thickness, and function, 1-2 weeks following treatment in patients with clinical improvement.[26]

Computed tomography

Cardiac involvement in CT chest is also uncommon and can only be seen in 1–5% of patients.[22] Presence of pericardial effusion and cardiomegaly have been reported in patients, with the former being more common.[2,3,23,24] In a patient presenting with acute ST-segment elevation, a CT coronary angiogram done had not shown any evidence of coronary stenosis.[26] Similarly, 18F-FDG PET CT study of 4 patients did not show any increased cardiac uptake. However, it reported mediastinal, right hilar, and supraclavicular lymphadenopathy.[29]

Cardiac magnetic resonance imaging (MRI)

Cardiac MRI showed evidence of increased wall thickness with diffuse biventricular hypokinesis along with severe left ventricular dysfunction in a symptomatic 53 year old patient. Marked biventricular myocardial interstitial edema was noted in short tau inversion recovery and T2-mapping sequences. Diffuse late gadolinium enhancement extending to the biventricular wall was also noted in phase-sensitive inversion recovery sequences, fulfilling the criteria for acute myocarditis. Circumferential pericardial effusion was noted, extending to 12 mm around the right cardiac chambers.[30]

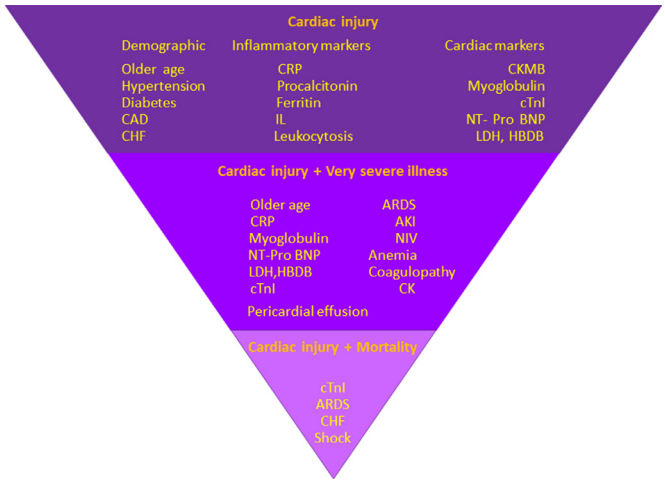

Fig. 2. Predictors of cardiac injury, severe illness, and mortality in COVID -19 patients.

Cardiac risk factors and COVID interaction

Studies have shown that patients with concomitant cardiovascular risk factors have worse clinical outcome. Onder etal from Italy found a case fatality of 7.2% among 22,000 COVID-19 patients. These patients also had higher cardiac risk factors including DM, ischemic heart disease, atrial fibrillation, advanced age, and prior stroke, seen in 35.5%, 30%, 24.5%, 20.2% and 9.6% respectively.[15] Additional risk factors which have been found in other studies are hypertension, obesity, and heart failure. The impact of smoking, dyslipidemia and obstructive sleep apnea are still being studied. Fig. 2 shows the various factors that have been independently linked with higher disease severity, multi-organ failure, requirement of invasive and noninvasive mechanical ventilation, presence of cardiac injury, and mortality.[4,8,14,15,17,21]

Treatment

Most treatment has been supportive. Various agents including antivirals, hydroxychloroquine, azithromycin, IL-6 receptor antagonist, and multiple other agents have been postulated as potential therapies.[1,6,14] The mortality benefit of these agents is yet to be established in clinical trials. Reported outcomes following the administration of corticosteroids and intravenous immunoglobulin are inconsistent. Concerns over the continuation of statins, angiotensin receptor blockers, ACE inhibitors in patients with prior cardiac comorbidities await vetting from further clinical evidence.[18] In the meanwhile, concerns deepen over QTC prolongation and risk of cardiac arrhythmias in patients receiving hydroxychloroquine, and azithromycin for treatment.[16]

Outcome

Mortality

Large population-based studies have reported variable mortality data, albeit higher as compared to seasonal flu. Wu et al. from China have reported a mortality of 2.3% whereas Onder et al. from Italy have reported a mortality of 7.2%.[8,15] The presence of cardiac comorbidities and cardiac involvement has been reported to be higher among patients with mortality.[4,21]

Predictors

Presence of comorbidities like hypertension, diabetes, heart failure, coronary artery disease are risk factors for cardiac involvement.[8] An elevated level of high-sensitive troponin, CPK, and LDH are risk factors for poor prognosis among patients with cardiac involvement.[17] Patients with cardiac injury are at higher risk of developing anemia, ARDS, AKI, coagulopathy, electrolyte imbalance, and need for noninvasive and invasive mechanical ventilation.[21] Patients with cardiac injury are also known to have high inflammatory markers, radiographic changes on CT, severe illness (based on SOFA score), multi-organ dysfunction, and higher mortality.[14] Among these, levels of high-sensitive troponin, a trend of rising high-sensitive troponin, elevated inflammatory markers suggesting cytokine storm, presence of previous cardiovascular comorbidities, and severity of infections are independently associated with increased mortality.[6,14,17,21] Fig. 2 depicts the reported predictors of cardiac injury, cardiac injury along with severe illness, and ultimately mortality.[31]

Limitation

At present most studies lack details of EKG, echocardiography at baseline, and after discharge. There is a paucity of studies comparing the outcomes in patients with and without cardiovascular comorbidities. Hence the findings of this report are skewed towards the subgroup of patients with significant cardiac involvement.[20] Details of the cardiovascular drugs and other medications affecting cardiovascular system are limited across all studies. Hence interaction of various cardiovascular drugs and their effect on outcome is unknown. Literature is even more limited when it comes to patients with cardiac transplants, congenital heart disease, or other specific subgroups including pregnancy.[18,32,33] With an increasing number of patients being affected, ongoing randomized clinical trials and future studies will be instrumental in providing additional clarifications. To keep this review more clinically relevant, we have not included the vast cardiovascular implications of this illness in terms of cardiac status during treatment, prevention in patients with cardiovascular comorbidities, drug interaction, and others. [34,35] However the strength of this review is in selectively including the published data of patients with COVID-19 only.[36]

Conclusion

Cardiac involvement is common in patients with COVID-19. Multiple mechanisms contribute to the two distinct patterns of cardiac injury. Prior cardiovascular comorbidities also contribute to increased cardiac involvement and poor outcome including mortality. Various markers of cardiac injury have been reported, high-sensitive troponin being proven to be of diagnostic and prognostic utility. Patients with cardiac injury have overall higher morbidity and mortality.

Ethical statement

The article doesn't contain the participation of any human being and animal.

Verification

All authors have seen the manuscript and agree to the content and data. All the authors played a significant role in the paper.

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Declaration of Competing Interest

Authors have no conflicts of interest to declare.

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References

1. Sahu KK, Mishra AK, Lal A. Novel coronavirus (2019-nCoV): update on 3rd coronavirus outbreak of 21st century. *QJM Mon J Assoc Physicians*. 2020(March). https://doi.org/10.1093/qjmed/hcaa081.
2. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. *Eur Radiol*. 2020. https://doi.org/10.1007/s00330-020-06801-0.
3. Sahu KK, Lal A, Mishra AK. An update on CT chest findings in coronavirus disease-19 (COVID-19). *Heart Lung J Crit Care*. 2020(March). https://doi.org/10.1016/j.hrtlng.2020.03.007.
4. Han H, Xie L, Liu R, et al. Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. *J Med Virol*. 2020(March). https://doi.org/10.1002/jmv.25809.
5. Deng Q, Hu B, Zhang Y, Wang H, Zhou X, Hu W, Cheng Y, Yan J, Ping H, Zhou Q. Suspected myocardial injury in patients with COVID-19: evidence from front-line clinical observation in Wuhan, China. *Int J Cardiol*. 2020. S0167-5273(20)31115-3.
6. Bansal M. Cardiovascular disease and COVID-19. *Diabetes Metab Syndr*. 2020;14(3):247–250. https://doi.org/10.1016/j.dsx.2020.03.013.
7. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus Disease 2019 in China. *N Engl J Med*. 2020;0(0). https://doi.org/10.1056/NEJMoa2002032.
8. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA*. 2020;323(13):1239–1242. https://doi.org/10.1001/jama.2020.2648.
9. Sahu KK, Lal A, Mishra AK. Latest updates on COVID-2019: a changing paradigm shift. *J Med Virol*. 2020(March). https://doi.org/10.1002/jmv.25760.
10. Perico L, Benigni A, Remuzzi G. Should COVID-19 concern nephrologists? Why and to what extent? The emerging impasse of angiotensin blockade. *Nephron*. 2020:(March):1–9. https://doi.org/10.1159/000507305.
11. Cheng H, Wang Y, Wang G-Q. Organ-protective effect of angiotensin-converting enzyme 2 and its effect on the prognosis of COVID-19. *J Med Virol*. 2020(March). https://doi.org/10.1002/jmv.25785.
12. Cao Y, Li L, Feng Z, et al. Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations. *Cell Discov*. 2020;6:11. https://doi.org/10.1038/s41421-020-0147-1.
13. Mishra AK, Sahu KK, Sargent J. Cardiac drugs and outcome in COVID - 19. *QJM Mon J Assoc Physicians*. 2020(April). Epub.
14. Driggin E, Madhavan MV, Bikdeli B, et al. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (COVID-19) pandemic. *J Am Coll Cardiol*. 2020(March). https://doi.org/10.1016/j.jacc.2020.03.031.
15. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020(March). https://doi.org/10.1001/jama.2020.4683.
16. Kapoor A, Pandurangi U, Arora V, et al. Cardiovascular risks of hydroxychloroquine in treatment and prophylaxis of COVID-19 patients: a scientific statement from the Indian Heart Rhythm Society [published online ahead of print, 2020 Apr 8]. *Indian Pacing Electrophysiol J*.. 2020. https://doi.org/10.1016/j.ipej.2020.04.003. S0972-6292(20)30038-3.
17. Clerkin Kevin J., Fried Justin A., R. Jayant, et al. Coronavirus disease 2019 (COVID-19) and cardiovascular disease. Circulation. 0 (0). doi:10.1161/CIRCULATIONAHA.120.046941.
18. Goldstein MR, Poland GA, Graeber CW. Are certain drugs associated with enhanced mortality in COVID-19? *QJM Mon J Assoc Physicians*. 2020(March). https://doi.org/10.1093/qjmed/hcaa103.
19. Lal A, Mishra AK, Sahu KK. CT chest findings in coronavirus disease-19 (COVID-19). *J Formos Med Assoc*. 2020(April). https://doi.org/10.1016/j.jfma.2020.03.010.
20. Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol*. 2020:(March):1–2. https://doi.org/10.1038/s41569-020-0360-5.
21. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020(March). https://doi.org/10.1001/jamacardio.2020.0950.
22. Wu J, Wu X, Zeng W, et al. Chest CT findings in patients with corona virus disease 2019 and its relationship with clinical features. *Invest Radiol*. 2020. https://doi.org/10.1097/RLI.0000000000000670. Publish Ahead of Print.
23. Xu X, Yu C, Qu J, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *Eur J Nucl Med Mol Imaging*. 2020(February). https://doi.org/10.1007/s00259-020-04735-9.
24. Li K, Wu J, Wu F, et al. The clinical and chest CT features associated with severe and critical COVID-19 Pneumonia. *Invest Radiol*. 2020. https://doi.org/10.1097/RLI.0000000000000672. Publish Ahead of Print.
25. Hanley B, Lucas SB, Youd E, Swift B, Osborn M. Autopsy in suspected COVID-19 cases. *J Clin Pathol*. 2020(March). https://doi.org/10.1136/jclinpath-2020-206522.
26. Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin. Eur Heart J. https://doi.org/10.1093/eurheartj/ehaa190.
27. Zeng JH, Liu Y-X, Yuan J, et al. First case of COVID-19 infection with fulminant myocarditis complication: case report and insights. March2020. https://doi.org/10.20944/preprints202003.0180.v1.
28. Sahu KK, Mishra AK, Lal A. A twin challenge to handle: COVID-19 with pregnancy. *J Med Virol*. 2020(April). https://doi.org/10.1002/jmv.25784.
29. Qin C, Liu F, Yen T-C, Lan X. 18F-FDG PET/CT findings of COVID-19: a series of four highly suspected cases. *Eur J Nucl Med Mol Imaging*. 2020;47(5):1281–1286. https://doi.org/10.1007/s00259-020-04734-w.
30. Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020(March). https://doi.org/10.1001/jamacardio.2020.1096.
31. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020(March). https://doi.org/10.1001/jamacardio.2020.1017.
32. Sahu KK, Lal A, Mishra AK. COVID-2019 and pregnancy: a plea for transparent reporting of all cases. *Acta Obstet Gynecol Scand*. 2020(March). https://doi.org/10.1111/aogs.13850.
33. Mishra AK, Sahu KK, Lal A. Patterns of heart Injury in COVID – 19 and relation to outcome. *J Med Virol*. 2020(April). https://doi.org/10.1002/jmv.25847.
34. Bonow RO, Fonarow GC, O'Gara PT, Yancy CW. Association of coronavirus disease 2019 (COVID-19) with myocardial injury and mortality. *JAMA Cardiol*. 2020(March). https://doi.org/10.1001/jamacardio.2020.1105.
35. Mishra AK, Sahu KK, Lal A. Reporting of all cardiac medications and their outcome in COVID - 19. *J Med Virol*. 2020(April). https://doi.org/10.1002/jmv.25843.
36. Sahu KK, Mishra AK, Lal A. COIVD 19 Disease: Tackling a pandemic in 21st Century. *QJM*. 2020(April).