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Review Article

Cardiomyopathy in COVID-19 Survivors: Mechanism, Management, and Prevention

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Abstract

Coronavirus disease (COVID-19) caused by infection of SARS-CoV-2 as of May 2020 has been confirmed in more than 3 million people, with more than 200 thousands deaths across the globe. It has been known that COVID-19 patients with underlying cardiovascular diseases and its risks including: hypertension, diabetes, coronary artery disease, and cerebrovascular diseases, may develop more severe respiratory track symptoms and requiring intensive care. Some patients may presenting with myocarditis or acute heart failure, which have high mortality and morbidity. There were evidences of myocardial Injury with an increase of troponin in one-third of those with COVID-19. It is conceivable that among those who recover from COVID-19 infection, there is a risk of developing cardiomyopathy in the future. Although there is no available study yet on chronic cardiac effects in COVID-19 survivors, there are some possible mechanisms of cardiomyopathy development as the COVID-19 sequelae. Optimal medical treatment especially during hospitalization and any comprehensive preventions should be taken to manage the risks of developing cardiomyopathy after discharge. These includes : providing best available COVID-19 drugs, cardiovascular medications and treatments, and other social preventive measures.

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Keyword: COVID-19, cardiomyopathy, myocarditis

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Introduction

Coronavirus disease of 2019 (COVID-19) is caused by new strain of coronavirus named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The first case of COVID-19 was started in Wuhan, China, then rapidly spread all over the world.[1] The World Health organization (WHO) have declared it as a pandemic. By May 2020 there were more than 4 millions people infected, with more than 250 thousands death reported across the globe.[2] Many of those having severe symptoms were with underlying cardiovascular diseases or its risks such as: hypertension, diabetes, coronary artery diseases, and cerebrovacular diseases.[1]

Early reports on patients with COVID-19 revealed that cardiac injury with elevated cardiac biomarkers, ECG changes, left ventricular dysfunction, including those described as cardiomyopathy were found in in the range of 12% to 33% patients.[1,3] Once those patients survive from the acute phase of infection, they may develop various extent of chronic cardiomyopathy. Recent recommendation on cardiovascular diseases and COVID-19 stated that pre-existing cardiovascular diseases may increase morbidity and mortality of patients with COVID-19, and warned that COVID-19 may cause serious cardiac sequelae. [4] reduced SARS-CoV-2 in swab samples.[4] Those combinations are known to prolong the QT interval and will increase the incident of Torsades de Pointes (TdP). The risk of TdP increases in critical patients,

Cardiomyopathy is a catasthropic condition of the heart leading for congestive heart failure (CHF), which increase risk of future mortality and morbidity.[4] Since we are in the mid of pandemic, there was no study yet on chronic effect of current COVID-19 for the development of cardiomypathy as sequelae. However we can learn from animal experimental in the past looking for cardiac sequela of coronavirus family infection focusing on development of cardiomyopathy.[5] It has also been known in human that viral infection such as coronavirus may result in myocarditis or heart dysfunction that lead to chronic cardiomyopathy as sequelae, once the patient survive. Along with recent findings on cardiac invovement following COVID-19, we may have insight on possible myocardial sequelae of those surviving from the disease course .

Given the close association between COVID-19 infection and myocardial injury, current review will highlight possible mechanisms and most importantly optimal management COVID-19 as well as other measures of prevention in order to reduce the extent of cardiomyopathy among the survivors. It is important to pay attention to this survivor population in the future, since they might be vulnerable of future events as well as chance of having re-infection.

Mechanisms of cardiomyopathy following Coronavirus infection

Study in the rabbit model of a coronavirus-induced dilated cardiomyopathy revealed that among animals that survive of coronavirus infection, there was an increase of heart mass, dilation of ventricle, myocite hyperthrophy, myocardial fibrosis, and myocarditis leading to development of dilated cardiomyopathy.[5] Development of ventricular dilation along with myocarditis and some degree of hypertrophy observed in all survivors with different degrees from mild to severe. Uniquely, there was more pronounced of Interstitial and replacement fibrosis in the papillary muscles.[5] All those findings suggested that coronavirus infection survivors may develop cardiomyopathy with different extents after an acute episode of the infection.

Coronavirus SARS-CoV-2 infected the host by attaching its protein spike at the surface of the virus to angiotensyn converting enzyme-2 (ACE-2) receptors. [6] ACE-2 was found in the lung alveolar epithelium, pericytes, cardiomyocytes, and enterocytes in the small intestine. Once the virus attached to the ACE-2 receptor at the lung alveolar, it then may cause pneumonia leading for acute severe acute respiratory distress syndrome as reported mostly during this pandemi.[6]

There were multiple possible mechanisms of cardiac injury leading to cardiomyopathy in COVID-19 as summarized at Figure 1: [6,7]

- COVID-19 may result in myocardial injury due to severe immune inflammatory response and cytokine storm.[8]
- Acute respiratory damage leading to hypoxia caused by pneumonia in COVID-19 could induce oxidative stress as well as myocardial injury due to increase of myocardial oxygen demand.
- Invasion of SARS-CoV-2 viral to the cardiomyocytes may causing direct toxic effect leading to

myocarditis.[9]

- Infection with SARS-CoV-2 may trigger microvascular dysfunction via its effects on ACE-2 receptor. This further causing tissue ischemia leading to ventricular dysfunction and/or arrhythmias.[7]

All those proposed mechanisms may result in myocardial fibrosis with various degree once the diseases recede. It may eventually cause cardiomyopathy sequelae with various clinical presentations.

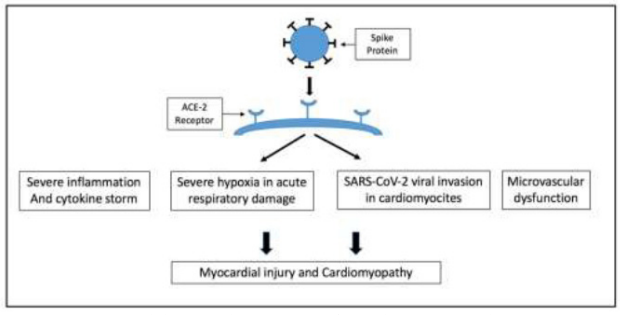

Figure 1. Possible mechanisms of cardiomyopathy in COVID-19

There was also a new term introduced as acute COVID-19 cardiovascular syndrome (AcovCS) in some patients presenting with myocarditis-like syndrome, that involving acute myocardial injury. It was associated with reduced left ventricular ejection fraction without evidence of obstructive coronary artery disease. This syndrome may be complicated with cardiac arrhythmias and/or clinical heart failure with or without associated hemodynamic instability including shock. [10]

More or less the mechanisms may be similar with those shown in Figure 1. Recent clinical data from China and US revealed that heart failure and cardiomyopathy although more frequent in non-survivors may be also be found as the sequelae among the survivors.[11] However, details on chronicity, type and class of heart failure In human with COVID-19 have not been consistently reported. Whether cases of cardiomyopathy exactly result from the underlying inflammatory state, hypoxia and hemodynamic impairment, or a direct effect of COVID-19, remains to be studied.[11]

Assessment for Cardiomyopathy in COVID-19

To assess COVID-19 patients with possibility of having cardiomyopathy or potential for its development in the future, currently no special guidelines available. However basic and common cardiovascular assessment shoud be performed. A risk and benefit consideration of doing an examination in COVID-19 patients should always be put in first place. Safety precausios of medical workers and the patients must be done first.

Once history and physical examinations were taken, further cardiac assesment would be required such as:

Electrocardiogram (ECG). Some COVID-19 patients may develop ECG changes ranging from ST elevation, ST depression, low voltage in the lim leads, and PVCs.[12] Although there is no specific changes for those with COVID-19, it is reasonable to incorporate the data with other examiantion and tests. For those with ECG changes along with other positive findings in other tests, thorough assessment and more intensive management may be required.

- **Blood test.** To assess cardiac involvement in COVID-19 patients laboratory testing for troponin and NT pro-BNP is required.[12] The other essential tests especially for those requiring hospital care might be including: C-reactive protein (CRP), ferritin, D-dimer, IL-6, and LDH, which were known elevated as response to SARS-CoV-2. The presence of these inflammatory biomarkers are associated with poor prognosis.[13]
- **Echocardiography.** Echocardiography can be useful to assess left and right ventricular structure and function, wall motion abnormalities, and to estimate cardiac hemodynamics. However, it is important to minimize sonographer time with COVID-19 positive patients to reduce the risk of spread. To this end, the decision to obtain an echocardiogram should be made on the basis of patient characteristics, blood test abnormalities, and hemodynamic stability and whether echocardiography information will make a difference in management.[7]
- **Other modalities.** To assess cardiac complication In center with capabilities, additional of doing more examination such as : cardiac magnetic resonance, endomyocardial biopsy and/or cardiac catheterization might be required if really necessary with cautions, given the risk to perform the examination in COVID-19 patients.[7]

Management of Cardiovascular Complications during Hospitalization for COVID-19

In regards to reduce the burden of possible chronic cardiomyopathy after an episode of acute COVID-19 requiring hospitalization, maximal therapy should be given for those showing signs of cardiac complications. Management of patients with COVID-19 have been described extensively in many reviews recently. [7,12,13] For severe COVID-19 with possible cardiac involvement optimal supportive care is very important. These include:

- Volume status and fluid resuscitation should be performed cautiously to avoid increase load in possible cardiomyopathy patients
- Maintaning targeted MAP by using proper inotropics if necessary
- Mechanical support /ECMO might be required in those with failing heart such as those with acute cardiomyopathy.[13]

In patients with acute cardiomyopathy in COVID-19 the severe symptoms usually happen during inflammatory period or interleukin storm. Optimal antiinflammatory and antiviral including hydroxychloroquine and azithromycin, anti-inflammatory therapies such as intravenous immune globulin (IVIG), tocilizumab, anakinra, and IV steroids. Antiviral therapy may include: remdesivir, lopinavir and ritonavir, have been used or considered in patients with COVID-19. [12,14] Caution should be given when using chroroquin since it may prolong QT interval, thus ECG evaluation should be performed in those receiving the drugs.

Use of ACE inhibitor and ARB has been a controversial issues given ACE-2 receptor known as entry site for coronavirus infection. A newest retrospective analysis in 1128 COVID-19 patients using ACE inhibitor and ARB concluded that in hospitalized COVID-19 patients with hypertension, use of ACEI/ARB lowering risk of all-cause mortality compared with ACEI/ARB non-users. While study interpretation needs to consider the potential for residual confounders. But the use ACE inhibitor should be balanced with hemodynamic and vital signs especially those in intensive care.[15]

Prevention

Since patients with underlying cardiovascular disease are at higher risk of morbidity and mortality, those patients should take great care in preventing of possible re-infection. That would increase the rate for possible cardiomyopathy development. This includes frequent handwashing, social distancing measures, proper and appropriate use of masks and cleaning and disinfecting commonly touched surfaces. If possible, the survivor patient should reduce outpatient visit and convert to telehealth visits to minimize risk of acquiring an infection in the nosocomial setting.[6]

Among those who survive from COVID-19. optimal medical therapy should be continued along with social distancing and personal hygiene. Given the newest study on the benefit of use ACE inhibitor and ARB in COVID-19 patients especially those with hypertension, it might be great hope that its benefit may be extended also to preserve cardiac function in cardiomyopathy post COVID-19 hospital care. However further study should be needed to resolve this issues.

Summary

Patients with COVID-19 may develop myocardial injury or myocarditis that lead to cardiomyopathy as the chronic sequelae of the disease. There are various possible mechanisms for the development of cardiomypathy after hospital care in patients recover from COVID-19. It is important to pay attention to this survivor group since the pandemic may be lasting for longer period. Optimal medical treatment and comprehensive prevention should be taken to manage those high risk patients of having cardiomyopathy during hospitalization as well as later at post-discharge period. These includes: providing best available COVID-19 drugs, cardiovascular medications and treatments, and other social preventive measures.

References

1. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
2. Coronavirus Resource Center, Johns Hopkins University, available at URL: https://coronavirus.jhu.edu/map.html

3. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020.
4. Zaman S, MacIsaac AI, Jennings GLR, et al. Cardiovascular disease and COVID-19: Australian/ New Zealand consensus statement. Med J of Australia. 2020.Online first, avalaible at URL https://www.mja.com.au/journal/2020/cardiovascular-disease-and-COVID-19-australiannew-zealand-consensus-statement
5. Alexander LK, Small JD, Edwards S, Baric RS. An experimental model for dilated cardiomyopathy after rabbit coronavirus infection. J Infect Dis. 1992;166(5):978-85.
6. Taan W, Aboulhosn J. The cardiovascular burden of coronavirus disease 2019 (COVID-19) with a focus on congenital heart disease . Int J Cardiol 2020, in press.
7. Schilling JD, Ravichandran AK, Mandras SA. Management of the hospitalized COVID-19 patient with acute cardiomyopathy or heart failure. Cardiology magazine of the American College. Apr 16, 2020.
8. Young BE, Ong SWX, Kalimuddin S, et al., Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore, JAMA (2020) 1–7, available at URL: http://www.ncbi.nlm.nih.gov/pubmed/ 32125362.
9. Xu JZ,Shi L,Wang Y,etal, Pathological findings ofCOVID-19 associated with acute respiratory distress syndrome, Lancet Respir Med. 2020; 2600 (20): 19–21
10. Hendren NS, Drazner MH, Bozkurt B, MD, Cooper LT. Description and Proposed Management of the Acute COVID-19 Cardiovascular Syndrome. Circulation. 2020; epub ahead of publishing.
11. Oren O, Kopecky SL, Gluckman TJ, et al. Coronavirus Disease 2019 (COVID-19): Epidemiology, Clinical Spectrum and Implications for the Cardiovascular Clinician. American College Cardiology expert analysis. 2020, available at https://www.acc.org/latest-in-cardiology/articles/2020/04/06/11/08/COVID-19-epidemiology-clinical-spectrum-and-implications-for-the-cv-clinician
12. Akhmerov A, Marban E. COVID-19 and the heart. Circ Res 2020;April 7:[Epub ahead of print].
13. Fried JA, Ramasubbu K, Bhatt R, et al. The variety of cardiovascular presentations of COVID-19. Circulation. 2020:[Epub ahead of print].
14. Li H, Zhou Y, Zhang M, Wang H, Zhao Q, Liu J. Updated approaches against SARS-CoV-
2. Antimicrob Agents Chemother. 2020; (Epub ahead of print).
15. Zhang P, Zhu L, Cai J et al. Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19. Circ Res. 2020; available at URL: https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.120.317134