



# Heart Failure and Coronavirus Disease-19

Refli Hasan\*

Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

## Abstract

Globally, 4.2% population suffer from heart failure. The condition has a mortality rate between 56% and 78%. Coronavirus disease-2019 (COVID-19) was first reported in December 2019 and became a pandemic since March 11, 2020. As COVID-19 emerges, cardiovascular disorders including, heart failure, become one of the most common comorbidity that increase the risk for contracting the disease. Heart failure and COVID-19 have reciprocal relationship. Patients with heart failure are at higher risk for COVID-19 with more unfavorable outcome. COVID-19 itself may deteriorate pre-existing heart failure in the subject. This situation is mediated by the presence of angiotensin converting enzyme-2 (ACE-2) in cardiac myocytes and pericytes, direct effect of viral invasion to myocytes and pericytes, downregulation of ACE-2 which hampers cardiovascular function, and uncontrolled inflammation known as cytokine storm. Prudent management, including implementation of telemedicine, continuation of ACE inhibitor and angiotensin receptor blocker, and medications' side effects monitoring, is important in managing patients with coexisting heart failure and COVID-19.

**Edited by:** Igor Spiroski  
**Citation:** Hasan R. Heart Failure and Coronavirus Disease-19. Open Access Maced J Med Sci. 2021 May 22;9(F):176-179. https://doi.org/10.3889/oamjms.2021.6124  
**Keywords:** Coronavirus disease-2019; Heart failure; Management; Telemedicine  
**\*Correspondence:** Refli Hasan, Department of Internal Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia. E-mail: refli\_hasan@yahoo.co.id  
**Received:** 02-Apr-2021  
**Revised:** 27-Apr-2021  
**Accepted:** 12-May-2021  
**Copyright:** © 2021 Refli Hasan  
**Funding:** This research did not receive any financial support  
**Competing Interests:** The authors have declared that no competing interests exist  
**Open Access:** This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

## Introduction

Approximately 64.3 million people or 4.2% of general population suffer from heart failure globally. Its prevalence is various across the globes such as 2.5% in USA, 3.5% in China, 4% in Germany, and 1.6% in UK while its incidence is reported to be 3.3 per 1000 person-years. 5-year mortality rate from heart failure ranges between 56% and 78% [1]. The mortality is reported to be lower in high income countries, which is 40–65%. In low- and middle-income countries, 2.2% of total hospital admissions are due to acute heart failure with mean in-hospital mortality of 8% [2].

Coronavirus disease-2019 (COVID-19) was first reported in Wuhan, China in December 2019. Since then, the disease spread throughout the world and was declared as a pandemic on March 11, 2020 by the World Health Organization [3], [4]. As per March 31, 2021, total cases of confirmed COVID-19 are 127,877,462 with 2,796,561 deaths. Americas and Europe are regions with the highest confirmed case number [5]. The etiology of the disease is a novel positive-sense single-stranded ribonucleic acid (RNA) beta-coronavirus, namely, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The virus belongs to *Coronaviridae* family [6], [7], [8], [9], [10], [11]. It is originally descended from bat and infecting human through intermediate reservoirs such as civet [12].

Cardiovascular disorder including heart failure and COVID-19 is interconnected. Subjects with

underlying cardiovascular disorders have increased risk for suffering from COVID-19. In the other hand, COVID-19 itself may deteriorate existing cardiovascular disorder in a patient [3], [6]. In addition, during the COVID-19 pandemic, the number of patients with heart failure visiting hospitals and health centers for routine follow-up is declining. As the consequence, patients are commonly admitted to hospital with more severe conditions and unfavorable outcome [13]. In this paper, we will discuss about the reciprocal relationship between heart failure and COVID-19.

## Brief COVID-19 Overview

COVID-19 is a disease caused by SARS-CoV-2 [14], [15], [16]. SARS-CoV-2 shares 96.2% of its property with bat coronavirus. The virus is round in shape with approximate diameter of 60–140 nm. Previously, coronaviruses have caused two disease outbreaks, namely, severe acute respiratory syndrome and Middle East respiratory syndrome [16]. The virus invades host's cell through angiotensin converting enzyme-2 (ACE-2) as the receptor [14], [15], [16], [17]. The spike glycoprotein (S protein) of the virus binds with ACE-2 and starts membrane fusion. The fusion is also facilitated by transmembrane serine protease 2. After the fusion, viral RNA is released into the host cell.

RNA will undergo translation into viral proteins. The proteins together with viral RNA are assembled to form new viruses and released from host cell through exocytosis. This process results in host cell damage and invasion of new cells [16], [18], [19]. Viral invasion also downregulates the ACE2 and stimulates renin-angiotensin-aldosterone system activation which promotes organ specific injury [19].

## Diagnosis of Heart Failure in COVID-19

The diagnosis of heart failure in COVID-19 is similar with the diagnosis in general population. Heart failure is a clinical syndrome and may be diagnosed clinically. Framingham criteria for heart failure were first published in 1971 and have been used widely. The diagnosis of heart failure is established if a patient has two major or one major plus two minor criteria concurrently (Table 1) [20].

**Table 1: Framingham criteria for diagnosis of heart failure**

| Major   | Minor   |
|---|---|
| 1. Paroxysmal nocturnal dyspnea   | 1. Ankle edema  |
| 2. Neck-vein distension (not counting supine position)  | 2. Night cough  |
| 3. Rales in the presence of unexplained dyspnea   | 3. Dyspnea on ordinary exertion                               |
| 4. Cardiomegaly and pulmonary hilar congestion (by X-ray in absence of left to right shunt), or increasing heart rate | 4. Hepatomegaly   |
| 5. Acute pulmonary edema described in hospital records  | 5. Pleural effusion   |
| 6. Ventricular gallop   | 6. Decreased vital capacity by one-third from maximum records |
| 7. Increased venous pressure (>16 cm H <sub>2</sub> O from right atrium)  | 7. Tachycardia (≥120 beats/min)                               |
| 8. Circulation time (>24 s, arm to tongue)  |   |
| 9. Hepatojugular reflux   |   |
| 10. Autopsy shows pulmonary edema, visceral congestion, cardiomegaly  |   |

Major or minor: Weight loss (≥4.5 kg) in 5 days, in response to heart failure therapy.

Further examination needed to evaluate cardiac function is echocardiography. Echocardiography is also important in assessing hemodynamic status of patients. Catheterization may be conducted as needed by always considering its risk and benefit since the disease is highly contagious [15]. In addition, auxiliary examinations related to heart failure in COVID-19 patients are significantly worse compared to the results in subjects without COVID-19. The level of cardiac biomarkers including N-terminal-proB-type natriuretic peptide, troponin-I, and creatine kinase-myocardial band is higher in deceased and severely infected COVID-19 patient [14], [15], [17]. Troponin level is also positively correlated with the presence of cardiovascular manifestations in patients with COVID-19 [17].

## Pathogenesis of Heart Failure in COVID-19

There are several pathogenesis underlying cardiovascular damage in COVID-19. ACE-2 is

present in alveolar epithelial cells, enterocytes, vascular endothelial cells, and cardiac myocytes and pericytes. This causes the presence of cardiovascular manifestations in COVID-19 [18], [21]. Direct effect of viral invasion causes damage to myocytes and pericytes. Downregulation of ACE-2 also causes diminishing of its protective effect against inflammation and fibrosis. In addition, diminished ACE-2 will increase the effect of angiotensin II and activation of renin-angiotensin-aldosterone system. Blood pressure will be dysregulated and uncontrolled. Increased coagulation state is observed in patients with COVID-19. Hypercoagulability tends to increase the risk of thrombus formation. If the thrombus obstructs coronary vessel, cardiac function will be impaired. Finally, uncontrolled inflammation in COVID-19 or widely known as cytokine storm hampers all organs' function including cardiovascular by deteriorating myocardial contraction and increases body's metabolic demand, particularly oxygen. Cardiovascular damage is represented as arrhythmia and myocarditis. Besides, increased metabolic demand may surpass the fulfillment ability of host's body. All of the conditions impair normal cardiac function and result in heart failure [1], [14], [15], [16], [17]. Heart failure itself can be deteriorated and causes cardiogenic shock. The incidence rate of cardiogenic shock in COVID-19 is reported to be 8% [16], [17].

## Association between Heart Failure and COVID-19

The disease course and outcome of COVID-19 are associated with the presence of comorbidities in each subject. Subjects with underlying comorbidities tend to suffer more severe course of COVID-19. Cardiovascular disease is one of the most common accompanying comorbidities in COVID-19 patients [13], [14], [15], [16], [17], [21]. Patients with existing cardiovascular disease have a mortality rate above 10% [15]. Another report stated that COVID-19 patients with heart failure had higher mortality rate compared to those who do not have heart failure with odds ratio of 1.42 [22]. Approximately 4–40% of COVID-19 patients have cardiovascular diseases as the comorbidity [14]. Furthermore, a quarter and one-third of patients admitted to hospital and intensive care unit, respectively, suffer from new onset of heart failure [15]. Pre-existing congestive heart failure and hypertension have been proven to increase in-hospital mortality of COVID-19 patients as high as 2.35 and 1.52 times, respectively. Furthermore, COVID-19 itself may cause new incidents of cardiovascular disease and deteriorate the existing ones [13], [14], [17]. COVID-19 increases the risk of acute cardiac injury and cardiac arrhythmia as high as 8.52 and 3.61 times higher [14]. Heart failure

is present as the complication of COVID-19 in 17.1–24.2% patients. Its incidence is significantly higher in critically ill patients compared to non-critically ill ones and in deceased patients compared to survivors [16]. Another study even reported a higher mortality rate in COVID-19 patients with heart failure, which was 64% [23].

The increased morbidity and mortality from COVID-19 in subjects with chronic heart failure (CHF) are caused by reduced immunity, general frailty, and hemodynamic incompetence to overcome the infection. Subjects with CHF produce more TNF- $\alpha$  and less IL-10 compared to normal subjects. COVID-19 itself triggers the release of pro-inflammatory cytokines; therefore, inflammatory response from COVID-19 becomes more severe. Severe inflammation requires high cardiac performance in which subjects with CHF are incapable of. This mechanism also causes exacerbation of chronic CHF [13], [15]. On the other hand, subjects with pre-existing cardiovascular diseases have elevated myocardial expression of ACE-2, causing higher viral invasion rate and worse outcomes [16].

## Management of Heart Failure in COVID-19

For patients with COVID-19 and heart failure, prudent utilization of intravenous fluid is mandatory. Optimal preload must be reached before adding inotropes [15]. The most common used medicine to manage heart failure in low- and middle-income countries are ACE inhibitors (57%), beta-blockers (34%), and mineralocorticoid receptor antagonists (32%) [2]. ACE inhibitor is safe in managing patients with COVID-19 and heart failure. Studies reported that ACE inhibitor does not worsen the disease course of COVID-19 [15], [16], [18]. ACE inhibitors do not cause increased ACE-2 expression [16]. Long-term utilization of ACE inhibitors is also not associated with increased susceptibility for contracting COVID-19 [18]. This is supported by findings of a study in Denmark. The study found that prior use of ACE inhibitors or angiotensin receptor blocker (ARB) did not significantly increase the susceptibility for suffering from COVID-19 nor worsen clinical course or outcome of COVID-19. Discontinuation of ACE inhibitor or ARB was not advised [21]. Another study from Sweden even reported that the use of ACE inhibitor or ARB gave protective effect against hospitalization or death from COVID-19 as much as 0.86 times compared to general population [19]. Vasopressors should be the last drug of choice [15].

Cardiovascular side effects of COVID-19 medications should be kept in mind [15]. Hydroxychloroquine is a potential cause of prolonged QT interval and torsades de pointes. Azithromycin, lopinavir/ritonavir, and favipiravir are also possess the

side effect of prolonged QT interval [15], [17]. Antivirals are also interact with warfarin which commonly consumed by heart failure patients with left ventricular assist devices. In case of cardiogenic shock, venovenous extracorporeal membrane oxygenation is proven effective [15].

Since lockdown is applied in almost all areas globally, further follow-up for patients with COVID-19 and heart failure becomes limited. This leads to delayed management of decompensation episodes together with difficulties in assessing therapeutic response. In addition, lifestyle changes during lockdown have increased the risk of decompensation [13]. For discharged COVID-19 patients with heart failure, remote monitoring is advisable. This method may reduce outpatient visits and decreases the possibility of disease transmission. Besides, remote monitoring will increase the patients' compliance [24]. Structured telephone support is the most simple and affordable method of remote monitoring. This method has been proven not to increase hospitalization in patients with heart failure. In patients with coexisting heart failure and COVID-19 with mild to moderate symptoms, this method is really useful both in maintaining home isolation and monitoring heart failure [13]. Virtual visits by video calls may be conducted in patients with stable heart failure. By virtual visits, inspection of clinical signs such as edema and jugular venous distension may be conducted. Remote monitoring does not increase the rate of emergency room visit, readmission, or death [13], [24]. Another option is home monitoring by health-care professionals. This approach provides more complete data including vital signs, physical examination, and simple auxiliary examinations [13], [15]. Utilization of advanced technology such as CardioMEMS offers particular benefits such as real time and continuous vital sign monitoring. However, direct outpatient clinic visit is still mandatory if the patient needs medical attention. Self-monitoring should be applied by all patients with heart failure including drug adherence, low-salt diet, and symptoms monitoring [15]. However, application of telemedicine methods should be accompanied by privacy protection since patient's confidential information is shared. The practice of telemedicine should follow local regulation regarding data encryption [13].

## Conclusion

Heart failure and COVID-19 possess reciprocal relationship. Heart failure increases the susceptibility of contracting COVID-19 and COVID-19 deteriorates pre-existing heart failure. The diagnosis of heart failure in subjects with COVID-19 is similar with general population. The presence of heart failure increases morbidity and mortality of COVID-19 patients. Prudent

management of heart failure in patient with COVID-19 including application of telemedicine is advised.

## References

- Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *Eur J Heart Fail.* 2020;22(8):1342-56. <https://doi.org/10.1002/ehf.1858>  
PMid:32483830
- Callender T, Woodward M, Roth G, Farzadfar F, Lemarie J, Gicquel S, *et al.* Heart failure care in low-and middle-income countries: A systematic review and meta-analysis. *PLoS Med.* 2014;11(8):e1001699. <https://doi.org/10.1371/journal.pmed.1001699>  
PMid:25117081
- Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, *et al.* Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol.* 2020;75(18):2352-71. <https://doi.org/10.1016/j.jacc.2020.03.031>  
PMid:32201335
- Ge H, Wang X, Yuan X, Xiao G, Wang C, Deng T, *et al.* The epidemiology and clinical information about COVID-19. *Eur J Clin Microbiol Infect Dis.* 2020;39(6):1011-9. <https://doi.org/10.1007/s10096-020-03874-z>  
PMid:32291542
- World Health Organization. Coronavirus Disease (COVID-19) Outbreak Situation. Geneva: World Health Organization; 2021. Available from: <http://www.covid19.who.int>. [Last accessed on 2021 Apr 01].
- Geng Y, Wei Z, Qian H, Huang J, Lodato R, Castriotta RJ. Pathophysiological characteristics and therapeutic approaches for pulmonary injury and cardiovascular complications of coronavirus disease 2019. *Cardiovasc Pathol.* 2020;47:107228. <https://doi.org/10.1016/j.carpath.2020.107228>  
PMid:32375085
- Ruslie RH, Darmadi D. Coronavirus disease-19 and mental health. *Open Access Maced J Med Sci.* 2020;8(1):268-71. <https://doi.org/10.3889/oamjms.2020.5304>
- Siregar GA, Siregar GP, Darmadi D, Ruslie RH. Coronavirus disease-19 and liver injury. *Open Access Maced J Med Sci.* 2020;8:154-7. <https://doi.org/10.3889/oamjms.2020.5028>
- Siregar GA, Siregar GP, Darmadi D. Gastrointestinal aspects of COVID-19: A review. *Open Access Maced J Med Sci.* 2020;8:52-4. <https://doi.org/10.3889/oamjms.2020.4891>
- Ruslie RH, Darmadi D, Siregar GA. Pediatric immunization practice during coronavirus disease-2019 pandemic. *Open Access Maced J Med Sci.* 2020;8:258-60. <https://doi.org/10.3889/oamjms.2020.5125>
- Ruslie RH, Darmadi D, Siregar GA. Susceptibility of coronavirus disease-19 in pediatric population. *Open Access Maced J Med Sci.* 2020;8:363-5. <https://doi.org/10.3889/oamjms.2020.5240>
- de Vries AA. SARS-CoV-2/COVID-19: A primer for cardiologists. *Neth Heart J.* 2020;28(7-8):366-83. <https://doi.org/10.1007/s12471-020-01475-1>  
PMid:32671650
- Tersalvi G, Winterton D, Cioffi GM, Ghidini S, Roberto M, Biasco L, *et al.* Telemedicine in heart failure during COVID-19: A step into the future. *Front Cardiovasc Med.* 2020;7:612818. <https://doi.org/10.3389/fcvm.2020.612818>  
PMid:33363223
- Dalia T, Lahan S, Ranka S, Acharya P, Gautam A, Goyal A, *et al.* Impact on congestive heart failure and role of cardiac biomarkers in COVID-19 patients. A systematic review and meta-analysis. *Indian Heart J.* 2021;73(1):91-8. <https://doi.org/10.1016/j.ihj.2020.12.002>  
PMid:33714416
- Bader F, Mania Y, Atallah B, Starling RC. Heart failure and COVID-19. *Heart Fail Rev.* 2021;26(1):1-10. <https://doi.org/10.1007/s10741-020-10008-2>  
PMid:32720082
- Lazaridis C, Vlachogiannis NI, Bakogiannis C, Spyridopoulos I, Stamatielopoulos K, Kanakakis I, *et al.* Involvement of cardiovascular system as the critical point in coronavirus disease 2019 (COVID-19) prognosis and recovery. *Hellenic J Cardiol.* 2020;61(6):381-95. <https://doi.org/10.1016/j.hjc.2020.05.004>  
PMid:32534109
- Shafi AM, Shaikh SA, Shirke MM, Iddawela S, Harky A. Cardiac manifestations in COVID-19 patients-a systematic review. *J Card Surg.* 2020;35(8):1988-2008. <https://doi.org/10.1111/jocs.14808>  
PMid:32652713
- Oz M, Lorke DE, Kabbani N. A comprehensive guide to the pharmacologic regulation of angiotensin converting enzyme 2 (ACE2), the SARS-CoV-2 entry receptor. *Pharmacol Ther.* 2020;221:107750. <https://doi.org/10.1016/j.pharmthera.2020.107750>  
PMid:33275999
- Savarese G, Benson L, Sundstrom J, Lund LH. Association between renin-angiotensin-aldosterone system inhibitor use and COVID-19 hospitalization and death: A 1.4 million patient nationwide registry analysis. *Eur J Heart Fail.* 2020;23(3):476-85. <https://doi.org/10.1002/ehf.2060>  
PMid:33222412
- Mahmood SS, Levy D, Vasan RS, Wang TJ. The Framingham heart study and the epidemiology of cardiovascular diseases: A historical perspective. *Lancet.* 2014;383(9921):999-1008. [https://doi.org/10.1016/s0140-6736\(13\)61752-3](https://doi.org/10.1016/s0140-6736(13)61752-3)  
PMid:24084292
- Fosbol EL, Butt JH, Ostergaard L, Andersson C, Selmer C, Kragholm K, *et al.* Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with COVID-19 diagnosis and mortality. *JAMA.* 2020;324(2):168-77. <https://doi.org/10.1001/jama.2020.11301>  
PMid:32558877
- Harrison SL, Fazio-Eynullayeva E, Lane DA, Underhill P, Lip GY. Comorbidities associated with mortality in 31,461 adults with COVID-19 in the United States: A federated electronic medical record analysis. *PLoS Med.* 2020;17(9):e1003321. <https://doi.org/10.1371/journal.pmed.1003321>  
PMid:32911500
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet.* 2020;395(10229):1054-62. [https://doi.org/10.1016/s0140-6736\(20\)30566-3](https://doi.org/10.1016/s0140-6736(20)30566-3)  
PMid:32171076
- Gorodeski EZ, Goyal P, Cox ZL, Thibodeau JT, Reay RE, Rasmusson K, *et al.* Virtual visits for care of patients with heart failure in the era of COVID-19: A statement from the heart failure society of America. *J Card Fail.* 2020;26(6):448-56. <https://doi.org/10.1016/j.cardfail.2020.04.008>  
PMid:32315732