**Name of Journal:** *World Journal of Virology*

**Manuscript NO:** 66004

**Manuscript Type:** OPINION REVIEW

**Heart failure in COVID-19 patients: Critical care experience**

John KJ *et al*. Heart failure in COVID-19 patients

Kevin John John, Ajay K Mishra, Chidambaram Ramasamy, Anu A George, Vijairam Selvaraj, Amos Lal

**Kevin John John,** Department of Critical Care, Believers Church Medical College Hospital, Thiruvalla 689103, India

**Ajay K Mishra, Chidambaram Ramasamy, Anu A George,** Department of Internal Medicine, Division of Cardiovascular Medicine, Saint Vincent Hospital, Worcester, MA 01608, United States

**Vijairam Selvaraj,** Division of Medicine, The Miriam Hospital and Warren Alpert Medical School of Brown University, Providence, RI 02906, United States

**Amos Lal,** Department of Medicine, Division of Pulmonary and Critical Care medicine, Mayo Clinic, Rochester, MN 55902, United States

**Author contributions:** John KJ, Lal A and Mishra AK were responsible for the conception and design of the work, screening of papers, data analysis and drafting the manuscript; Ramasamy C and George AA were responsible for the literature review; Selvaraj V, Lal A and Mishra AK reviewed and revised the preliminary draft; Lal A gave the final approval for the published version of the manuscript.

**Corresponding author: Amos Lal, FACP, MBBS, Assistant Professor,** Department of Medicine, Division of Pulmonary and Critical Care medicine, Mayo Clinic, 200 First st, SW, Rochester, MN 55902, United States. lal.amos@mayo.edu

**Received:** March 19, 2021

**Revised:** May 9, 2021

**Accepted:** November 25, 2021

**Published online:** January 25, 2022

**Abstract**

Patients with heart failure (HF) may be at a higher risk of coronavirus disease 2019 (COVID-19) infection and may have a worse outcome due to their comorbid conditions and advanced age. In this narrative review, we aim to study the interaction between COVID-19 and HF from a critical care perspective. We performed a systematic search for studies that reported HF and critical care-related outcomes in COVID-19 patients in the PubMed and Medline databases. From a total of 1050 papers, we identified 26 that satisfied the eligibility criteria for our review. Data such as patient demographics, HF, intensive care unit (ICU) admission, management, and outcome were extracted from these studies and analyzed. We reported outcomes in heart-transplant patients with COVID-19 separately. In hospitalized patients with COVID-19, the prevalence of HF varied between 4% and 21%. The requirement for ICU admission was between 8% and 33%. HF patients with COVID-19 had an overall mortality rate between 20% and 40%. We identified that HF is an independent predictor of mortality in hospitalized COVID-19 patients, and patients with HF were more likely to require ventilation, ICU admission and develop complications. Patients with HF with reduced ejection fraction did worse than those with HF with midrange ejection fraction, and HF with preserved ejection fraction. COVID-19 patients with HF should be identified early and managed aggressively in an attempt to improve outcomes in this cohort of patients.

**Key Words:** Heart failure; COVID-19; Critical care; Intensive care; Mortality

**©The** **Author(s) 2022.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** John KJ, Mishra AK, Ramasamy C, George AA, Selvaraj V, Lal A. Heart failure in COVID-19 patients: Critical care experience. *World J Virol* 2022; 11(1): 1-19

**URL:** <https://www.wjgnet.com/2220-3249/full/v11/i1/1.htm>

**DOI:** https://dx.doi.org/10.5501/wjv.v11.i1.1

**Core Tip:** Heart failure (HF) can lead to worse outcomes in coronavirus disease 2019 (COVID-19). Moreover, critically ill patients with COVID-19 can develop *de novo* HF. Patients with COVID-19 and HF are more likely to require ventilation, ICU admission and develop complications. HF is an independent predictor of mortality in hospitalized COVID-19 patients and therefore, HF should be identified early and managed aggressively in an attempt to improve outcomes in critically ill patients.

**INTRODUCTION**

Coronavirus disease 2019 (COVID-19) emerged from China in December of 2019 and continues to be a public health emergency of international concern. As of March 12, 2021, more than 118 million cases have been diagnosed worldwide with 29.3 million patients reported from the United States. Patients with pre-existing comorbidities, cardiac dysfunction and immunocompromised status continue to be at high risk of morbidity and mortality. The literature on COVID-19 infection in patients with heart failure (HF) is limited. Patients with HF may be at higher risk of COVID-19 infection and have a worse outcome due to their comorbid conditions and advanced age.

The currently available literature regarding the role of critical care and a multidisciplinary approach in treating patients with HF and COVID-19 infection, remains scarce. In this narrative review, we aim to study the interaction between COVID-19 and HF from a critical care perspective. We also aim to explore the various outcomes as reported in the literature in this subgroup of patients and to provide a summary of the current evidence and practices in the management of HF in COVID-19 patients in the intensive care unit (ICU).

In this review, we have attempted to summarize all the articles published on the presentation and management of patients with COVID-19 and HF. We searched the PubMed and Medline database for the MeSH terms “COVID-19”, “heart failure" and” critical care”. Studies published in English, including adults with HF and COVID-19 infection were eligible to be included in this review (Figure 1). All studies published before March 2021 were included. Studies that provided details on patient demographics, HF, ICU admission, management, and outcome were analyzed. Various treatment details including medications such as beta blockers, angiotensin converting enzyme inhibitors (ACEi), aldosterone receptor blockers (ARB), angiotensin receptor-neprilysin inhibitors (ARNi), automatic implantable cardioverter-defibrillator, permanent pace-maker and cardiac resynchronization therapy were included. Critical care details that were obtained were the type of organ dysfunction, the requirement of non-invasive and invasive ventilation, administration of vasopressor support, extra-corporeal membrane oxygenation (ECMO) and outcome. Articles that did not have the patient’s details, opinions, comments, letters, and articles not published in English were excluded from the analysis. Studies that included cardiac transplant patients were analyzed separately. Two independent clinicians reviewed all articles.

As of March 2021, a total of 1050 papers were identified (Figure 1). Among these, 26 satisfied the eligibility criteria for our study. One study was a prospective cohort study, while all others were retrospective studies. Studies were principally published from North American and European nations. There were significant differences in the study design, data collection and measured outcomes among the studies which made the comparison of data difficult. Therefore, we divided the studies into four categories and reported the outcomes separately. The four categories were: (1) Studies highlighting prevalence of HF, requirement of ICU level of care and outcomes in hospitalized COVID-19 patients; (2) Studies reporting outcomes in COVID-19 patients admitted to ICU; (3) Studies reporting outcomes in HF patients with COVID-19; and (4) Studies reporting outcomes in heart-transplant patients with COVID-19 (Figure 2).

**INCREASED RISK OF HEART FAILURE IN COVID-19 PATIENTS**

Among studies that reported outcomes in hospitalized patients with COVID-19, we found 11 studies that provided data on HF and ICU admission (Table 1)[1-11]. The total number of patients in this group was 9420, with studies from the United States contributing the maximum number of patents. The diagnosis of COVID-19 was uniformly established with reverse transcription polymerase chain reaction (RT-PCR) in all of the patients. The proportion of patients with pre-existing HF varied from 1% to 21%, which was almost ten times the community prevalence of HF, as reported by the Framingham study[12]. This suggests that patients with HF are more likely to require hospitalization for COVID-19. Zylla *et al*[3] reported that 3% of patients developed newly diagnosed (*de novo)* left ventricular (LV) dysfunction after admission, while Zhou *et al*[9]and Chen *et al*[10] reported a number close to 25%. This highlights the fact that HF can be both a risk factor, as well as a complication of COVID-19. Most studies reported a male preponderance with a mean age above 60 years. The requirement for ICU admission was between 8% and 33%. Patients with HF were more likely to require mechanical ventilation and develop complications such as thrombo-embolism, sepsis, stroke and acute kidney injury. The overall mortality rate for hospitalized patients with COVID-19 was between 4% and 40%. Inciardi *et al*[1] noted that chronic therapy with an ACEi, ARB, or ARNI had to be discontinued in 77% of cases because of severe hypotension, and patients who died were more likely to have a history of HF. In the same study, the mortality rate remained higher in patients with cardiac disease compared to those without (26% *vs* 9%; *P* = 0.039), even after excluding patients who were denied intubation due to comorbidities or age. Another study used multivariate regression modelling to identify an increased risk of atrial fibrillation among COVID-19 patients with HF (RR 1.88; *P* = 0.023), which in-turn increased the odds of ICU or intermediate care ward admission (OR 2.37; 95%CI: 1.10-5.09; *P* = 0.03)[4,5]. HF was also linked to brady-arrhythmias (OR 9.75; 95%CI: 1.95-48.65) by a separate group of investigators[5]. Three separate meta-analysis identified that HF was independently associated with an increased risk of mortality in patients with COVID-19[13-15].

**NEED FOR INTENSIVE CARE UNIT LEVEL OF CARE**

We found six studies that reported HF data in COVID-19 patients who were admitted to the ICU, while excluding patients who were hospitalized without requiring ICU care (Table 2)[5,16-20]. These studies had a total patient number of 6539, with a major patient population contributed from the United States. The mean age in this group of patients was above 60 years and there were more men than women. Between 10% and 43% of these patients had pre-existing HF. This range was higher than what was observed among hospitalized patients overall. It was also noted that more patients developed *de-novo* HF in this group (up to 33%)[16]. The average ICU length of stay was between 2 to 5 weeks and a majority of patients required ventilatory assistance. In addition, advanced life-sustaining supportive interventions such as ECMO were also utilized by 3% to 15% of these patients. As a group, these patients had a higher mortality rate, which was as high as 52%. A cross-sectional observational multi-centre nationwide survey in Italy identified that obesity, chronic kidney disease and hypertension in men, and obesity (OR 2.564; 95%CI: 1.336-4.920; *P* < 0.0001) and HF (OR 1.775; 95%CI: 1.030-3.057) in women were associated with higher rate of ICU admission[19]. Similar observations were made from a single academic medical centre in New York City and Long Island which found that the strongest risk factors for critical illness besides age were HF (OR 1.9; 95%CI: 1.4-2.5), BMI > 40 (OR 1.5; 95%CI: 1.0-2.2), and male sex (OR 1.5; 95%CI: 1.3-1.8)[17].

**OUTCOMES IN CRITICALLY ILL COVID-19 PATIENTS WITH PRE-EXISTING HEART FAILURE**

There were five studies (from North America and Europe) that focused on the outcomes of COVID-19 infection in patients with pre-existing HF (Table 3)[21-25]. Three of them were from the United States, one was from Italy and the last one was from Denmark. Together, these studies included 9191 patients. Maximum number of patients were contributed by the study by Bhatt *et al*[21]. The mean age of patients in these studies were above 70 years, which was about 10 years higher than what was observed in the two previous groups. Two out of the five studies had more women than men. This was in contrast to the uniform male predominance observed in the two previous groups. ICU admission rates were reported by two studies and ranged between 23% and 29%. ECMO was used by three patients in one study[21]. An overall mortality rate between 20% to 40% was observed. Overall mortality variation in multinational studies have ranged from close to 30 % to over 90 %. There was also a significant inter-hospital variability in the outcome of critically ill patients which could not be attributed to the location or performance of the treating facility[26]. Tomasoni *et al*[24] reported more in-hospital complications such as acute HF (33.3% *vs* 5.1%, *P* < 0.001), acute renal failure (28.1% *vs* 12.9%, *P* < 0.001), multiorgan failure (15.9% *vs* 5.8%, *P* = 0.004) and sepsis (18.4% *vs* 8.9%, *P* = 0.006) in COVID-19 patients with a prior history of HF. This suggests that patients with HF and COVID-19 have a poorer outcome than the general population. When compared to hospital admissions for other causes, HF patients admitted for COVID-19 were older, more likely to identify as Black and/or Hispanic, had higher rates of diabetes and kidney disease and used more healthcare resources such as ICU beds (29% *vs* 15%), mechanical ventilation (17% *vs* 6%), and central venous catheter insertion (19% *vs* 7%; *P* < 0.001 for all)[21]. They also had higher in-hospital mortality (24.2% *vs* 2.6%) as well as higher skilled-nursing and rehabilitative care requirement among survivors (13% *vs* 41%)[21]. Similar conclusions were drawn by Alvarez-Garcia *et al*[22], who noted that the history of HF was an independent risk factor for the need for ICU care (adjusted OR 1.71; 95%CI: 1.25-2.34; *P* = 0.001), intubation and mechanical ventilation (adjusted OR 3.64; 95%CI: 2.56 -5.16; *P* < 0.001), and in-hospital mortality (adjusted OR 1.88; 95%CI: 1.27-2.78; *P* = 0.002). Furthermore, the former was the only study to look at outcomes stratified by left ventricular ejection fraction (LVEF) and found that cardiogenic shock (7.8% *vs* 2.3% *vs* 2%; *P* = 0.019) and HF-related causes for 30-day readmission (47.1% *vs* 0% *vs* 8.6%) were significantly higher in patients with HF with reduced ejection fraction (HFrEF) than in those with HF with midrange ejection fraction (HFmrEF) or HF with preserved ejection fraction (HFpEF)[22]. Multivariate cox regression identified older age, more severe HF [baseline New York Heart Association (NYHA) functional classes III and IV], previous mitral regurgitation, lower systolic blood pressure, lower oxygen saturation, lower lymphocyte count, and increased troponin concentrations as risk factors for in-hospital mortality in COVID-19 patients with HF[22].

**DATA ON CARDIAC TRANSPLANT PATIENTS WITH COVID-19**

We analyzed studies that included heart transplant patients separately because they are a distinct subset of patients who are likely to be on immunosuppressive therapy. We found five retrospective studies with a total of 99 patients (Table 4)[27-31]. This was a group of predominantly male patients with a mean age above 55 years and a wide variation in requirements for ICU level of care; ranging from 10.5% to 100%. The patients who were admitted to ICU were sicker as evidenced by increased requirement of vasopressors, mechanical ventilation, and renal replacement therapy (83% *vs* 38%)[28]. The mortality rate was between 18% and 37%. In one study, all patients who required ICU admission died[29]. This was higher than the mortality rate in the general population, but not much more than non-transplanted HF patients or patients in ICU. Bottio *et al*[31] reported that older age (*P* = 0.002), diabetes mellitus (*P* = 0.040), extracardiac arteriopathy (*P* = 0.040), previous percutaneous coronary intervention (*P* = 0.040), cardiac allograft vasculopathy score (*P* = 0.039), lower glomerular filtration rate (*P* = 0.004), and higher NYHA functional classes (*P* = 0.023) were all significantly associated with in-hospital mortality among heart-transplant patients with COVID-19[31]. We know that steroids are beneficial in severe COVID-19, and cardiac transplant patients are often on multiple immunosuppressive medications that include steroids, calcineurin inhibitors and anti-metabolites[32]. Whether these immunosuppressive medications protected these patients from severe disease is a question that warrants further investigation.

In this review, we summarized the relationship between HF, COVID-19 and the role of intensive care in patients with COVID-19 and HF. Our review of literature revealed many interesting observations. The evidence suggests that patients with HF are more likely to be hospitalized after COVID-19 infection. Exact quantification of risk will require community-level studies and cannot be derived from the hospital-based studies included in this review. Also, patients with COVID-19 are at increased risk of developing *de novo* HF after admission to the hospital; a risk that increases substantially with admission to the ICU. The reversibility and long-term morbidity of COVID-19 related *de* novo HF is unclear at this point and will require future studies with longer durations of follow up. Patients with COVID-19 and HF had increased chance of requiring ICU admission, mechanical ventilation, vasopressors and renal replacement therapy. They also had more complications and a higher mortality rate when compared to non-HF patients. These differences may be due to the effect of additional organ injury and decreased physiologic reserve leading to faster decompensation. This may also be an indirect marker for variation in practices. While it is expected that patients admitted to the ICU are at increased risk for development of complications and mortality, what is interesting is that the presence of HF represents an additional independent risk factor for the same. Furthermore, due to the similarity in clinical presentation, HF in COVID-19 patients is probably underdiagnosed. Therefore, it stands to reason that the risk estimate from the studies reported thus far are lower than the true risk estimate. It was noteworthy that the outcomes in critically ill heart transplant patients with COVID-19 was not very different from critically ill non-heart transplant patients. Whether the immunosuppressive medications that heart transplant patients are on, provides them with a selective advantage in combating the ‘cytokine storm’ seen in COVID-19 is a question worth asking. What is clear from our analysis of the existing literature is that HF is inextricably linked with the outcomes of COVID-19 infection. What is not known is the exact mechanisms by which they are linked and therefore, this is a field with immense scope for future research. There are many reasons to study HF in COVID-19 patients. Heart-lung interactions dictate that insult to one organ, affects the other. Acute respiratory distress syndrome (ARDS) is the most common manifestation of severe COVID-19 disease. While hypoxia and positive pressure ventilation stresses the right heart, the left heart has to compensate for increased metabolic demand. These problems are compounded in patients with pre-existing HF. Therefore, it is vital that we investigate the interaction between HF and COVID-19 so that we have a better understanding of its pathophysiology, optimal management and outcome.

**PATHOGENESIS OF HF IN COVID-19**

Cardiac troponins were elevated in 8%-12% of COVID-19 cases and the percentage rose up to 23%-33% in critically ill patients[1,33,34]. COVID-19 is theorized to injure the myocardium indirectly and directly. The systemic inflammatory response and cytokine storm increases blood viscosity and coagulability, which causes endothelial dysfunction[35,36]. The sympathetic activation, tachycardia, increased myocardial oxygen consumption and energy expenditure can also injure the myocardium. More cases of takotsubo cardiomyopathy are being diagnosed in patients with severe COVID-19[37]. Elevated positive end-expiratory pressure during mechanical ventilation in COVID-19 patients with severe ARDS increases right ventricular wall stress and can further reduce the cardiac output in a failing heart[38]. In a series of consecutive autopsy cases, Lindner and colleagues documented SARS-CoV-2 in 24 of 39 patients (61.5%), suggesting that direct viral myocardial damage is also possible[39]. SARS-CoV-2 attaches to human cells after binding with its spikes to the ACE2, which are upregulated in patients with cardiovascular disease, diabetes, and those treated with ACEi or ARB[40-42]. In light of this observation, role of ACE2 and ACEi in the pathogenesis of COVID-19 related myocardial injury has also been investigated from a therapeutic point of view.

While there are multiple factors contributing to HF in COVID-19, the incidence of true ‘myocarditis’ in COVID-19 in unclear[43]. Some authors estimate that myocarditis may account for up to 7% of COVID-19 deaths[44]. This estimate is fundamentally flawed because the diagnosis cannot be confirmed in a vast number of cases. Also, the presentation of acute coronary syndrome, sepsis-related cardiomyopathy and takotsubo cardiomyopathy can mimic myocarditis, making this a challenging diagnosis. Myocarditis, even when subclinical, can worsen patient outcomes. In the short term, it can increase the risk of arrythmias and precipitate decompensated HF, especially in patients with pre-existing chronic HF[45]. In the long term, the resultant myocardial fibrosis and negative remodeling can accelerate the decline of systolic function leading to a limitation of physical activity. Therefore, in the ICU, it is important to screen patients for subclinical myocarditis, by following the AHA recommendation of testing patients with signs consistent with myocarditis with one or more cardiac imaging methods such as echocardiogram or cardiovascular magnetic resonance[46].

**SCREENING FOR HF IN THE ICU**

Up to one-third of COVID-19 patients admitted to the ICU develop cardiomyopathy, and cohort studies from Wuhan have estimated the proportion of COVID-19 patients with cardiac injury to be between 20% and 28%[8,47]. Therefore, it would be prudent to screen all COVID-19 patients admitted to the ICU for HF. Critically ill patients in the ICU, are not able to communicate their complaints, and physical examination findings are often limited. A screening algorithm such as the one suggested by the Cardiac Society of Australia and New Zealand can be employed in the ICU[48]. Incorporation of such a screening algorithm into the treatment protocol will help identify more patients with HF and optimize treatment.

Although major society guidelines recommend the measurement of natriuretic peptides when the diagnosis of HF is uncertain, they should be interpreted in the context of other clinical information due to their high sensitivity and limited specificity[49,50]. In addition to its diagnostic value, natriuretic peptides also have prognostic significance with higher pro-brain natriuretic peptide (pro-BNP) values associated with increased mortality[51,52]. Therefore, natriuretic peptides can be used for risk stratification of COVID-19 patients with HF. Elevations in cardiac troponins have also been observed in COVID-19 patients and may indicate both coronary and non-coronary disease[53]. Acute coronary syndrome, microvascular ischemia, myocarditis, takotsubo cardiomyopathy and arrythmia are some of the reasons for an elevated troponin in COVID-19 patients[54]. While this makes the measurement of cardiac troponins less useful from the point of view of diagnosing HF, an elevated troponin level cannot be ignored as it may point towards underlying heart disease in an asymptomatic COVID-19 patient.

**ROLE OF CARDIAC POINT OF CARE ULTRASOUND**

The American Society of Echocardiography defines cardiac point of care ultrasound (POCUS) as ‘focused exams with specific imaging protocols based upon suspicion of a specific disease’ and differentiates it from ultrasound assisted physical examination[55]. POCUS has multiple uses in the diagnosis and management of HF in COVID-19 patients in the ICU. POCUS has the added benefit of reducing risk of exposure to the health-care worker, when compared to the use of stethoscopes[56]. Adhering to a set-protocol such as the one described by Huang *et al*[57]*,* will reduce inter and intra-observer variability.Documenting POCUS findings is important and if possible, the images should be stored on the device or on a central server. As this technology is relatively new, using mannequins for standardized training in image acquisition and interpretation may be helpful[58].

**ECHOCARDIOGRAPHY**

The American Society of Echocardiography, in a statement endorsed by the American College of Cardiology, recommends that Transthoracic echocardiography should be performed if it is expected to provide clinical benefit[59]. In the ICU, this can be done at the bedside, with adequate airborne precautions[59]. Echocardiography (ECHO) can provide more information when compared to cardiac POCUS and can also be used to risk stratify patients to aid in follow up. A study of 75 hospitalized patients with COVID-19 showed a significant association between lower LVEF and mortality[60]. The mortality among the patients with LVEF < 50% was 65% compared to 26% in the group with LVEF ≥ 50%. The patients with LVEF < 50% also had higher troponin T and pro-BNP levels[60]. Stepwise modelling demonstrated that mechanical ventilation (OR 22.6; 95%CI: 3.0-170.4), LVEF < 50% (OR 8.2; 95%CI: 1.4-46.9), and pro-BNP above the cohort median value (OR 5.8; 95%CI: 1.4-23.9) were the strongest predictors of mortality[60]. Similar findings were reported by Alvarez-Garcia *et al*[22], as mentioned previously. Both left ventricular global longitudinal strain (HR 1.39; 95%CI: 1.11-1.76) and right ventricular longitudinal strain (HR 1.33; 95%CI: 1.15-1.53) were associated with increased mortality in COVID-19[61,62]. ECHO also allows for more detailed evaluation of right heart function, including tricuspid annular plane systolic excursion/pulmonary artery systolic pressure ratio (HR 0.026; 95%CI: 0.01-0.579; *P* = 0.019) which was an independent predictor of mortality in one study[63].

**MANAGEMENT OF ACUTE HEART FAILURE IN THE ICU**

Management of acute HF in COVID-19 patients in the ICU should be done according to established guidelines and protocols. Although questions have been raised about the potential deleterious effects of ACEi and ARBs in COVID-19, a joint statement from the Heart Failure Society of America and American College of Cardiology/American Heart Association recommends continuation of these medications in patients with HF, if hemodynamics allow[64]. An effort must be made to identify HF due to takotsubo cardiomyopathy, which may masquerade as an acute coronary syndrome, but is increasingly being recognized in the context of COVID-19[37]. Since catecholamine-excess is considered to be part of the pathogenesis behind takotsubo cardiomyopathy, this subset of patients may benefit from restricting the use of catecholamine-inotropes such as dobutamine and dopamine and replacing them with non-catecholamine inotropes such as levosimendan and milrinone[65-67]. In patients who develop HF refractory to inotrope support, mechanical circulatory support, *e.g.*, veno-arterial ECMO or other cardiac assistive devices such as Impella (Abiomed, Danvers, MA, United States) may be used. These interventions are resource intensive and may not be available in all centres. In patients with suspected myocarditis or cytokine mediated injury, high dose corticosteroids, intravenous immunoglobulin and even selective cytokine blockade are options that can be considered on an experimental basis, given the absence of strong evidence of their benefit[68].

**EXTRA-CORPOREAL MEMBRANE OXYGENATION**

The World Health Organization has recommended that ECMO can be used in experienced centres for the management of critically ill COVID-19 patients with ARDS with or without HF[69]. The Extracorporeal Life Support Organization has emphasized that ECMO should be judiciously used as a rescue strategy in severely ill patients since it is a resource-intensive, highly specialized, and expensive form of life support with the potential for significant complications[70]. Key considerations while implementing ECMO include proper patient assessment and selection, personnel assignment, infection control measures before and during ECMO initiation as well as devising protocols for ECMO weaning, decannulation and rehabilitation[71]. Given the resource intensive nature of ECMO, some authors have raised the question of whether it is worth using during a pandemic[72]. Barbaro *et al*[73] used the data from the ELSO registry and determined that the mortality in COVID-19 patients who required ECMO was less than 40%. This shows that in the appropriate setting, ECMO is indeed beneficial in critically ill COVID-19 patients.

The role of ECMO after CPR (E-CPR) is unclear at this point, and as of February 3, 2021, the Extracorporeal Life Support Organization registry has reported 32 COVID-19 patients who underwent E-CPR[74]. Current guidelines recommend judicious use of E-CPR and only in centres that already have experience in its use[70,75,76]. Candidate selection should be done with due consideration of the patients comorbidities, other organ function, short and long-term life expectancy, availability of ECMO resources and risk of infectious exposure during cannulation and bed-side management[71].

**LEFT-VENTRICULAR ASSIST DEVICES**

Literature on left ventricular assist devices and COVID-19 are scant. LVADs have been used with varying success in the management of HF in COVID-19. Valchanov *et al*[77] have described a case of a 43-year patient with severe COVID-19 ARDS and HF who was managed with veno-arterial ECMO and an Impella 5.0 ventricular assist device. The patient, however, succumbed to his illness after a 3-wk period. There are case-reports and case-series of patients on long-term LVAD who developed COVID-19[78-82]. It is important to recognize that COVID-19 patients with LVADs are particularly prone to thrombotic complications. This requires intensivists to walk a fine line between potential complications of bleeding and thrombosis. In recipients with COVID-19 infection, daily interrogation of LVAD parameters can help in the early recognition of early signs of hemodynamic compromise, pump thrombosis, right ventricular failure, vasoplegia associated with secondary infection, or innate device malfunction[83].

**REHABILITATION OF HF PATIENTS WITH COVID-19 AFTER ICU DISCHARGE**

Rehabilitation of COVID-19 survivors who were in the ICU is critical. In those who developed HF, this becomes even more important. COVID-19 survivors who were critically ill often develop respiratory sequelae, cognitive sequelae, deconditioning, critical-illness related myopathy and neuropathy, dysphagia, joint stiffness and pain and psychiatric problems[84,85]. An early physical medicine and rehabilitation consultation, will help identify and address these issues early on. Rehabilitation can be initiated while the patient is still in ICU. However, more holistic rehabilitation will require assessment of respiratory capacity, muscle strength, exercise capacity, gait speed, balance and activities of daily living[86]. This is preferably done in a dedicated rehabilitation facility, after the patient is discharged home[82]. A graded exercise-based cardiac rehabilitation strategy can be prescribed, in accordance with standard HF guidelines[87].

Home based cardiac rehabilitation programs with telemonitoring methods can also be considered[88]. Few authors have reported promising results with remote cardiac care during the COVID-19 pandemic with telemonitoring devices such as the V-LAP™ (Vectorious Medical Technologies, Ltd) device for monitoring left atrial pressure as well as the HeartLogic platform (Boston Scientific, Marlborough, Massachusetts)[89,90]. Although this technology is relatively new, we may soon see its integration into rehabilitation protocols for patients with HF, after ICU discharge.

**LIMITATIONS**

We identified that only very few studies discussed the medical management of sick patients with COVID-19 in the background of HF. While many studies reported prevalence of ‘cardiovascular disease’ and ‘cardiac injury’ (usually defined as troponin I above the 99th percentile upper reference limit or new abnormalities shown on electrocardiography and echocardiography) in COVID-19 patients, the number of studies that reported chronic and *de novo* HF in this cohort was limited. Part of the reason may be the similarity in presentation of severe COVID-19 ARDS and acute decompensated HF. This is particularly challenging in the ICU patients, in whom both conditions often coexist. Moreover, HF is both a risk factor and a complication of COVID-19. Moreover, studies included in this review were retrospective and lack granular details on the severity of the disease, medical treatment, comorbidities, drug interactions, and outcome. Details of COVID-19 infection on the management of HF and vice versa were also not uniformly addressed. Outcomes in different studies were different. Details of treatment of COVID-19, duration of therapy, length of hospital stay, the long-term outcome were not uniformly available. Details of intensive care treatment, including mode of ventilation, pressors of choice, renal replacement therapies, the role of sedatives and paralytics on this subgroup of populations were also not discussed in all studies. However, the strength of the studies was that it included studies with patients having COVID-19 in the background of HF from all over the world. We also tried to identify the predictors of morbidity and the role of intensive care therapy in these patients, from the literature. More research focusing on this subset of patients is necessary to clarify the pathogenesis, improve screening methods and identify optimal therapeutic strategies.

**CONCLUSION**

In this review, we identified that HF is an independent predictor of mortality in hospitalized COVID-19 patients. Patients with HF were more likely to require ventilation, ICU admission and develop complications. Patients with HFrEF did worse than those with HFmrEF and HFpEF. COVID-19 patients with HF should be identified early and managed aggressively in an attempt to improve outcomes in this cohort of patients.

**REFERENCES**

1 **Inciardi RM**, Adamo M, Lupi L, Cani DS, Di Pasquale M, Tomasoni D, Italia L, Zaccone G, Tedino C, Fabbricatore D, Curnis A, Faggiano P, Gorga E, Lombardi CM, Milesi G, Vizzardi E, Volpini M, Nodari S, Specchia C, Maroldi R, Bezzi M, Metra M. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J* 2020; **41**: 1821-1829 [PMID: 32383763 DOI: 10.1093/eurheartj/ehaa388]

2 **Singer AJ**, Morley EJ, Meyers K, Fernandes R, Rowe AL, Viccellio P, Thode HC, Bracey A, Henry MC. Cohort of Four Thousand Four Hundred Four Persons Under Investigation for COVID-19 in a New York Hospital and Predictors of ICU Care and Ventilation. *Ann Emerg Med* 2020; **76**: 394-404 [PMID: 32563601 DOI: 10.1016/j.annemergmed.2020.05.011]

3 **Zylla MM**, Merle U, Vey JA, Korosoglou G, Hofmann E, Müller M, Herth F, Schmidt W, Blessing E, Göggelmann C, Weidner N, Fiedler MO, Weigand MA, Kälble F, Morath C, Leiner J, Kieser M, Katus HA, Thomas D. Predictors and Prognostic Implications of Cardiac Arrhythmias in Patients Hospitalized for COVID-19. *J Clin Med* 2021; **10** [PMID: 33401735 DOI: 10.3390/jcm10010133]

4 **Russo V**, Di Maio M, Mottola FF, Pagnano G, Attena E, Verde N, Di Micco P, Silverio A, Scudiero F, Nunziata L, Fele N, D'Andrea A, Parodi G, Albani S, Scacciatella P, Nigro G, Severino S. Clinical characteristics and prognosis of hospitalized COVID-19 patients with incident sustained tachyarrhythmias: A multicenter observational study. *Eur J Clin Invest* 2020; **50**: e13387 [PMID: 32813877 DOI: 10.1111/eci.13387]

5 **Bhatla A**, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, Moss J, Chahal AA, Anesi G, Denduluri S, Domenico CM, Arkles J, Abella BS, Bullinga JR, Callans DJ, Dixit S, Epstein AE, Frankel DS, Garcia FC, Kumareswaram R, Nazarian S, Riley MP, Santangeli P, Schaller RD, Supple GE, Lin D, Marchlinski F, Deo R. COVID-19 and cardiac arrhythmias. *Heart Rhythm* 2020; **17**: 1439-1444 [PMID: 32585191 DOI: 10.1016/j.hrthm.2020.06.016]

6 **Peltzer B**, Manocha KK, Ying X, Kirzner J, Ip JE, Thomas G, Liu CF, Markowitz SM, Lerman BB, Safford MM, Goyal P, Cheung JW. Outcomes and mortality associated with atrial arrhythmias among patients hospitalized with COVID-19. *J Cardiovasc Electrophysiol* 2020; **31**: 3077-3085 [PMID: 33017083 DOI: 10.1111/jce.14770]

7 **Lala A**, Johnson KW, Januzzi JL, Russak AJ, Paranjpe I, Richter F, Zhao S, Somani S, Van Vleck T, Vaid A, Chaudhry F, De Freitas JK, Fayad ZA, Pinney SP, Levin M, Charney A, Bagiella E, Narula J, Glicksberg BS, Nadkarni G, Mancini DM, Fuster V; Mount Sinai COVID Informatics Center. Prevalence and Impact of Myocardial Injury in Patients Hospitalized With COVID-19 Infection. *J Am Coll Cardiol* 2020; **76**: 533-546 [PMID: 32517963 DOI: 10.1016/j.jacc.2020.06.007]

8 **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; **5**: 802-810 [PMID: 32211816 DOI: 10.1001/jamacardio.2020.0950]

9 **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**: 1054-1062 [PMID: 32171076 DOI: 10.1016/S0140-6736 (20)30566-3]

10 **Chen T**, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H, Wang T, Guo W, Chen J, Ding C, Zhang X, Huang J, Han M, Li S, Luo X, Zhao J, Ning Q. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020; **368**: m1091 [PMID: 32217556 DOI: 10.1136/bmj.m1091]

11 **Jarrett M**, Schultz S, Lyall J, Wang J, Stier L, De Geronimo M, Nelson K. Clinical Mortality in a Large COVID-19 Cohort: Observational Study. *J Med Internet Res* 2020; **22**: e23565 [PMID: 32930099 DOI: 10.2196/23565]

12 **Ho KK**, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: the Framingham Study. *J Am Coll Cardiol* 1993; **22**: 6A-13A [PMID: 8376698 DOI: 10.1016/0735-1097 (93)90455-a]

13 **Ssentongo P**, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: A systematic review and meta-analysis. *PLoS One* 2020; **15**: e0238215 [PMID: 32845926 DOI: 10.1371/journal.pone.0238215]

14 **Chidambaram V**, Tun NL, Haque WZ, Majella MG, Sivakumar RK, Kumar A, Hsu AT, Ishak IA, Nur AA, Ayeh SK, Salia EL, Zil-E-Ali A, Saeed MA, Sarena APB, Seth B, Ahmadzada M, Haque EF, Neupane P, Wang KH, Pu TM, Ali SMH, Arshad MA, Wang L, Baksh S, Karakousis PC, Galiatsatos P. Factors associated with disease severity and mortality among patients with COVID-19: A systematic review and meta-analysis. *PLoS One* 2020; **15**: e0241541 [PMID: 33206661 DOI: 10.1371/journal.pone.0241541]

15 **Shoar S**, Hosseini F, Naderan M, Mehta JL. Meta-analysis of Cardiovascular Events and Related Biomarkers Comparing Survivors Versus Non-survivors in Patients With COVID-19. *Am J Cardiol* 2020; **135**: 50-61 [PMID: 32916148 DOI: 10.1016/j.amjcard.2020.08.044]

16 **Zeng JH**, Wu WB, Qu JX, Wang Y, Dong CF, Luo YF, Zhou D, Feng WX, Feng C. Cardiac manifestations of COVID-19 in Shenzhen, China. *Infection* 2020; **48**: 861-870 [PMID: 32725595 DOI: 10.1007/s15010-020-01473-w]

17 **Petrilli CM**, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Francois F, Horwitz LI. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ* 2020; **369**: m1966 [PMID: 32444366 DOI: 10.1136/bmj.m1966]

18 **Hayek SS**, Brenner SK, Azam TU, Shadid HR, Anderson E, Berlin H, Pan M, Meloche C, Feroz R, O'Hayer P, Kaakati R, Bitar A, Padalia K, Perry D, Blakely P, Gupta S, Shaefi S, Srivastava A, Charytan DM, Bansal A, Mallappallil M, Melamed ML, Shehata AM, Sunderram J, Mathews KS, Sutherland AK, Nallamothu BK, Leaf DE; STOP-COVID Investigators. In-hospital cardiac arrest in critically ill patients with covid-19: multicenter cohort study. *BMJ* 2020; **371**: m3513 [PMID: 32998872 DOI: 10.1136/bmj.m3513]

19 **Iaccarino G**, Grassi G, Borghi C, Carugo S, Fallo F, Ferri C, Giannattasio C, Grassi D, Letizia C, Mancusi C, Minuz P, Perlini S, Pucci G, Rizzoni D, Salvetti M, Sarzani R, Sechi L, Veglio F, Volpe M, Muiesan ML; SARS-RAS Investigators. Gender differences in predictors of intensive care units admission among COVID-19 patients: The results of the SARS-RAS study of the Italian Society of Hypertension. *PLoS One* 2020; **15**: e0237297 [PMID: 33022004 DOI: 10.1371/journal.pone.0237297]

20 **Arentz M**, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, Lee M. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA* 2020; **323**: 1612-1614 [PMID: 32191259 DOI: 10.1001/jama.2020.4326]

21 **Bhatt AS**, Jering KS, Vaduganathan M, Claggett BL, Cunningham JW, Rosenthal N, Signorovitch J, Thune JJ, Vardeny O, Solomon SD. Clinical Outcomes in Patients With Heart Failure Hospitalized With COVID-19. *JACC Heart Fail* 2021; **9**: 65-73 [PMID: 33384064 DOI: 10.1016/j.jchf.2020.11.003]

22 **Alvarez-Garcia J**, Lee S, Gupta A, Cagliostro M, Joshi AA, Rivas-Lasarte M, Contreras J, Mitter SS, LaRocca G, Tlachi P, Brunjes D, Glicksberg BS, Levin MA, Nadkarni G, Fayad Z, Fuster V, Mancini D, Lala A. Prognostic Impact of Prior Heart Failure in Patients Hospitalized With COVID-19. *J Am Coll Cardiol* 2020; **76**: 2334-2348 [PMID: 33129663 DOI: 10.1016/j.jacc.2020.09.549]

23 **Caraballo C**, McCullough M, Fuery MA, Chouairi F, Keating C, Ravindra NG, Miller PE, Malinis M, Kashyap N, Hsiao A, Wilson FP, Curtis JP, Grant M, Velazquez EJ, Desai NR, Ahmad T. COVID-19 infections and outcomes in a live registry of heart failure patients across an integrated health care system. *PLoS One* 2020; **15**: e0238829 [PMID: 32997657 DOI: 10.1371/journal.pone.0238829]

24 **Tomasoni D**, Inciardi RM, Lombardi CM, Tedino C, Agostoni P, Ameri P, Barbieri L, Bellasi A, Camporotondo R, Canale C, Carubelli V, Carugo S, Catagnano F, Dalla Vecchia LA, Danzi GB, Di Pasquale M, Gaudenzi M, Giovinazzo S, Gnecchi M, Iorio A, La Rovere MT, Leonardi S, Maccagni G, Mapelli M, Margonato D, Merlo M, Monzo L, Mortara A, Nuzzi V, Piepoli M, Porto I, Pozzi A, Sarullo F, Sinagra G, Volterrani M, Zaccone G, Guazzi M, Senni M, Metra M. Impact of heart failure on the clinical course and outcomes of patients hospitalized for COVID-19. Results of the Cardio-COVID-Italy multicentre study. *Eur J Heart Fail* 2020; **22**: 2238-2247 [PMID: 33179839 DOI: 10.1002/ejhf.2052]

25 **Andersson C**, Gerds T, Fosbøl E, Phelps M, Andersen J, Lamberts M, Holt A, Butt JH, Madelaire C, Gislason G, Torp-Pedersen C, Køber L, Schou M. Incidence of New-Onset and Worsening Heart Failure Before and After the COVID-19 Epidemic Lockdown in Denmark: A Nationwide Cohort Study. *Circ Heart Fail* 2020; **13**: e007274 [PMID: 32482087 DOI: 10.1161/CIRCHEARTFAILURE.120.007274]

26 **Domecq JP**, Lal A, Sheldrick CR, Kumar VK, Boman K, Bolesta S, Bansal V, Harhay MO, Garcia MA, Kaufman M, Danesh V, Cheruku S, Banner-Goodspeed VM, Anderson HL 3rd, Milligan PS, Denson JL, St Hill CA, Dodd KW, Martin GS, Gajic O, Walkey AJ, Kashyap R; Society of Critical Care Medicine Discovery Viral Infection and Respiratory Illness Universal Study (VIRUS): COVID-19 Registry Investigator Group. Outcomes of Patients With Coronavirus Disease 2019 Receiving Organ Support Therapies: The International Viral Infection and Respiratory Illness Universal Study Registry. *Crit Care Med* 2021; **49**: 437-448 [PMID: 33555777 DOI: 10.1097/CCM.0000000000004879]

27 **Latif F**, Farr MA, Clerkin KJ, Habal MV, Takeda K, Naka Y, Restaino S, Sayer G, Uriel N. Characteristics and Outcomes of Recipients of Heart Transplant With Coronavirus Disease 2019. *JAMA Cardiol* 2020; **5**: 1165-1169 [PMID: 32402056 DOI: 10.1001/jamacardio.2020.2159]

28 **Ketcham SW**, Adie SK, Malliett A, Abdul-Aziz AA, Bitar A, Grafton G, Konerman MC. Coronavirus Disease-2019 in Heart Transplant Recipients in Southeastern Michigan: A Case Series. *J Card Fail* 2020; **26**: 457-461 [PMID: 32417380 DOI: 10.1016/j.cardfail.2020.05.008]

29 **Singhvi A**, Barghash M, Lala A, Mitter SS, Parikh A, Oliveros E, Rollins BM, Brunjes DL, Alvarez-Garcia J, Johnston E, Ryan K, Itagaki S, Moss N, Pinney SP, Anyanwu A, Mancini D. Challenges in heart transplantation during COVID-19: A single-center experience. *J Heart Lung Transplant* 2020; **39**: 894-903 [PMID: 32891266 DOI: 10.1016/j.healun.2020.06.015]

30 **Lima B**, Gibson GT, Vullaganti S, Malhame K, Maybaum S, Hussain ST, Shah S, Majure DT, Wallach F, Jang K, Bijol V, Esposito MJ, Williamson AK, Thomas RM, Bhuiya TA, Fernandez HA, Stevens GR. COVID-19 in recent heart transplant recipients: Clinicopathologic features and early outcomes. *Transpl Infect Dis* 2020; **22**: e13382 [PMID: 32583620 DOI: 10.1111/tid.13382]

31 **Bottio T**, Bagozzi L, Fiocco A, Nadali M, Caraffa R, Bifulco O, Ponzoni M, Lombardi CM, Metra M, Russo CF, Frigerio M, Masciocco G, Potena L, Loforte A, Pacini D, Faggian G, Onorati F, Sponga S, Livi U, Iacovoni A, Terzi A, Senni M, Rinaldi M, Boffini M, Marro M, Jorgji V, Carrozzini M, Gerosa G. COVID-19 in Heart Transplant Recipients: A Multicenter Analysis of the Northern Italian Outbreak. *JACC Heart Fail* 2021; **9**: 52-61 [PMID: 33309578 DOI: 10.1016/j.jchf.2020.10.009]

32 **Sterne JAC**, Murthy S, Diaz JV, Slutsky AS, Villar J, Angus DC, Annane D, Azevedo LCP, Berwanger O, Cavalcanti AB, Dequin PF, Du B, Emberson J, Fisher D, Giraudeau B, Gordon AC, Granholm A, Green C, Haynes R, Heming N, Higgins JPT, Horby P, Jüni P, Landray MJ, Le Gouge A, Leclerc M, Lim WS, Machado FR, McArthur C, Meziani F, Møller MH, Perner A, Petersen MW, Savovic J, Tomazini B, Veiga VC, Webb S, Marshall JC; WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. *JAMA* 2020; **324**: 1330-1341 [PMID: 32876694 DOI: 10.1001/jama.2020.17023]

33 **Wang D**, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020; **323**: 1061-1069 [PMID: 32031570 DOI: 10.1001/jama.2020.1585]

34 **Yang X**, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; **8**: 475-481 [PMID: 32105632 DOI: 10.1016/S2213-2600 (20)30079-5]

35 **Tomasoni D**, Italia L, Adamo M, Inciardi RM, Lombardi CM, Solomon SD, Metra M. COVID-19 and heart failure: from infection to inflammation and angiotensin II stimulation. Searching for evidence from a new disease. *Eur J Heart Fail* 2020; **22**: 957-966 [PMID: 32412156 DOI: 10.1002/ejhf.1871]

36 **Mishra AK**, Sahu KK, Lal A, Sargent J. Patterns of heart injury in COVID-19 and relation to outcome. *J Med Virol* 2020; **92**: 1747 [PMID: 32267000 DOI: 10.1002/jmv.25847]

37 **John K**, Lal A, Mishra A. A review of the presentation and outcome of takotsubo cardiomyopathy in COVID-19. *Monaldi Arch Chest Dis* 2021; **91** [PMID: 33759445 DOI: 10.4081/monaldi.2021.1710]

38 **Luecke T**, Pelosi P. Clinical review: Positive end-expiratory pressure and cardiac output. *Crit Care* 2005; **9**: 607-621 [PMID: 16356246 DOI: 10.1186/cc3877]

39 **Lindner D**, Fitzek A, Bräuninger H, Aleshcheva G, Edler C, Meissner K, Scherschel K, Kirchhof P, Escher F, Schultheiss HP, Blankenberg S, Püschel K, Westermann D. Association of Cardiac Infection With SARS-CoV-2 in Confirmed COVID-19 Autopsy Cases. *JAMA Cardiol* 2020; **5**: 1281-1285 [PMID: 32730555 DOI: 10.1001/jamacardio.2020.3551]

40 **Yan R**, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Science* 2020; **367**: 1444-1448 [PMID: 32132184 DOI: 10.1126/science.abb2762]

41 **Ferrario CM**, Jessup J, Chappell MC, Averill DB, Brosnihan KB, Tallant EA, Diz DI, Gallagher PE. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. *Circulation* 2005; **111**: 2605-2610 [PMID: 15897343 DOI: 10.1161/CIRCULATIONAHA.104.510461]

42 **Mishra AK**, Sahu KK, Sargent J. Cardiac drugs and outcome in COVID-19. *QJM* 2020; **113**: 523-524 [PMID: 32289168 DOI: 10.1093/qjmed/hcaa127]

43 **Mishra AK**, Lal A, Sahu KK, Sargent J. Cardiovascular factors predicting poor outcome in COVID-19 patients. *Cardiovasc Pathol* 2020; **49**: 107246 [PMID: 32640385 DOI: 10.1016/j.carpath.2020.107246]

44 **Driggin E**, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, Brown TS, Der Nigoghossian C, Zidar DA, Haythe J, Brodie D, Beckman JA, Kirtane AJ, Stone GW, Krumholz HM, Parikh SA. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. *J Am Coll Cardiol* 2020; **75**: 2352-2371 [PMID: 32201335 DOI: 10.1016/j.jacc.2020.03.031]

45 **Siripanthong B**, Nazarian S, Muser D, Deo R, Santangeli P, Khanji MY, Cooper LT Jr, Chahal CAA. Recognizing COVID-19-related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm* 2020; **17**: 1463-1471 [PMID: 32387246 DOI: 10.1016/j.hrthm.2020.05.001]

46 **Kociol RD**, Cooper LT, Fang JC, Moslehi JJ, Pang PS, Sabe MA, Shah RV, Sims DB, Thiene G, Vardeny O; American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. Recognition and Initial Management of Fulminant Myocarditis: A Scientific Statement From the American Heart Association. *Circulation* 2020; **141**: e69-e92 [PMID: 31902242 DOI: 10.1161/CIR.0000000000000745]

47 **Guo T**, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol* 2020; **5**: 811-818 [PMID: 32219356 DOI: 10.1001/jamacardio.2020.1017]

48 **Lal S**, Hayward CS, De Pasquale C, Kaye D, Javorsky G, Bergin P, Atherton JJ, Ilton MK, Weintraub RG, Nair P, Rudas M, Dembo L, Doughty RN, Kumarasinghe G, Juergens C, Bannon PG, Bart NK, Chow CK, Lattimore JD, Kritharides L, Totaro R, Macdonald PS. COVID-19 and Acute Heart Failure: Screening the Critically Ill - A Position Statement of the Cardiac Society of Australia and New Zealand (CSANZ). *Heart Lung Circ* 2020; **29**: e94-e98 [PMID: 32418875 DOI: 10.1016/j.hlc.2020.04.005]

49 **Lindenfeld J**, Albert NM, Boehmer JP, Collins SP, Ezekowitz JA, Givertz MM, Katz SD, Klapholz M, Moser DK, Rogers JG, Starling RC, Stevenson WG, Tang WH, Teerlink JR, Walsh MN. Heart Failure Society of America. HFSA 2010 Comprehensive Heart Failure Practice Guideline. *J Card Fail* 2010; **16**: e1-194 [PMID: 20610207 DOI: 10.1016/j.cardfail.2010.04.004]

50 **Yancy CW**, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL; Writing Committee Members. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013; **128**: e240-e327 [PMID: 23741058 DOI: 10.1161/CIR.0b013e31829e8776]

51 **Maisel AS**, Duran JM, Wettersten N. Natriuretic Peptides in Heart Failure: Atrial and B-type Natriuretic Peptides. *Heart Fail Clin* 2018; **14**: 13-25 [PMID: 29153197 DOI: 10.1016/j.hfc.2017.08.002]

52 **Hsich EM**, Grau-Sepulveda MV, Hernandez AF, Eapen ZJ, Xian Y, Schwamm LH, Bhatt DL, Fonarow GC. Relationship between sex, ejection fraction, and B-type natriuretic peptide levels in patients hospitalized with heart failure and associations with inhospital outcomes: findings from the Get With The Guideline-Heart Failure Registry. *Am Heart J* 2013; **166**: 1063-1071.e3 [PMID: 24268222 DOI: 10.1016/j.ahj.2013.08.029]

53 **Gaze DC**. Clinical utility of cardiac troponin measurement in COVID-19 infection. *Ann Clin Biochem* 2020; **57**: 202-205 [PMID: 32255359 DOI: 10.1177/0004563220921888]

54 **Chapman AR**, Bularga A, Mills NL. High-Sensitivity Cardiac Troponin Can Be an Ally in the Fight Against COVID-19. *Circulation* 2020; **141**: 1733-1735 [PMID: 32251612 DOI: 10.1161/CIRCULATIONAHA.120.047008]

55 **Kirkpatrick JN**, Grimm R, Johri AM, Kimura BJ, Kort S, Labovitz AJ, Lanspa M, Phillip S, Raza S, Thorson K, Turner J. Recommendations for Echocardiography Laboratories Participating in Cardiac Point of Care Cardiac Ultrasound (POCUS) and Critical Care Echocardiography Training: Report from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2020; **33**: 409-422.e4 [PMID: 32122742 DOI: 10.1016/j.echo.2020.01.008]

56 **Buonsenso D**, Pata D, Chiaretti A. COVID-19 outbreak: less stethoscope, more ultrasound. *Lancet Respir Med* 2020; **8**: e27 [PMID: 32203708 DOI: 10.1016/S2213-2600 (20)30120-X]

57 **Huang G**, Vengerovsky A, Morris A, Town J, Carlbom D, Kwon Y. Development of a COVID-19 Point-of-Care Ultrasound Protocol. *J Am Soc Echocardiogr* 2020; **33**: 903-905 [PMID: 32624091 DOI: 10.1016/j.echo.2020.04.023]

58 **Sheehan FH**, Otto CM, Freeman RV. Echo simulator with novel training and competency testing tools. *Stud Health Technol Inform* 2013; **184**: 397-403 [PMID: 23400191 DOI: 10.3233/978-1-61499-209-7-397]

59 **Kirkpatrick JN**, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE Statement on Protection of Patients and Echocardiography Service Providers During the 2019 Novel Coronavirus Outbreak: Endorsed by the American College of Cardiology. *J Am Soc Echocardiogr* 2020; **33**: 648-653 [PMID: 32503700 DOI: 10.1016/j.echo.2020.04.001]

60 **Faridi KF**, Hennessey KC, Shah N, Soufer A, Wang Y, Sugeng L, Agarwal V, Sharma R, Sewanan LR, Hur DJ, Velazquez EJ, McNamara RL. Left Ventricular Systolic Function and Inpatient Mortality in Patients Hospitalized with Coronavirus Disease 2019 (COVID-19). *J Am Soc Echocardiogr* 2020; **33**: 1414-1415 [PMID: 32951969 DOI: 10.1016/j.echo.2020.08.016]

61 **Janus SE**, Hajjari J, Karnib M, Tashtish N, Al-Kindi SG, Hoit BD. Prognostic Value of Left Ventricular Global Longitudinal Strain in COVID-19. *Am J Cardiol* 2020; **131**: 134-136 [PMID: 32732008 DOI: 10.1016/j.amjcard.2020.06.053]

62 **Li Y**, Li H, Zhu S, Xie Y, Wang B, He L, Zhang D, Zhang Y, Yuan H, Wu C, Sun W, Zhang Y, Li M, Cui L, Cai Y, Wang J, Yang Y, Lv Q, Zhang L, Xie M. Prognostic Value of Right Ventricular Longitudinal Strain in Patients With COVID-19. *JACC Cardiovasc Imaging* 2020; **13**: 2287-2299 [PMID: 32654963 DOI: 10.1016/j.jcmg.2020.04.014]

63 **D'Alto M**, Marra AM, Severino S, Salzano A, Romeo E, De Rosa R, Stagnaro FM, Pagnano G, Verde R, Murino P, Farro A, Ciccarelli G, Vargas M, Fiorentino G, Servillo G, Gentile I, Corcione A, Cittadini A, Naeije R, Golino P. Right ventricular-arterial uncoupling independently predicts survival in COVID-19 ARDS. *Crit Care* 2020; **24**: 670 [PMID: 33256813 DOI: 10.1186/s13054-020-03385-5]

64 **Bozkurt B**, Kovacs R, Harrington B. Joint HFSA/ACC/AHA Statement Addresses Concerns Re: Using RAAS Antagonists in COVID-19. *J Card Fail* 2020; **26**: 370 [PMID: 32439095 DOI: 10.1016/j.cardfail.2020.04.013]

65 **Veillet-Chowdhury M**, Hassan SF, Stergiopoulos K. Takotsubo cardiomyopathy: a review. *Acute Card Care* 2014; **16**: 15-22 [PMID: 24552225 DOI: 10.3109/17482941.2013.869346]

66 **Papanikolaou J**, Tsolaki V, Makris D, Zakynthinos E. Early levosimendan administration may improve outcome in patients with subarachnoid hemorrhage complicated by acute heart failure. *Int J Cardiol* 2014; **176**: 1435-1437 [PMID: 25147072 DOI: 10.1016/j.ijcard.2014.08.039]

67 **Mrozek S**, Srairi M, Marhar F, Delmas C, Gaussiat F, Abaziou T, Larcher C, Atthar V, Menut R, Fourcade O, Geeraerts T. Successful treatment of inverted Takotsubo cardiomyopathy after severe traumatic brain injury with milrinone after dobutamine failure. *Heart Lung* 2016; **45**: 406-408 [PMID: 27402629 DOI: 10.1016/j.hrtlng.2016.06.007]

68 **Mehta P**, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020; **395**: 1033-1034 [PMID: 32192578 DOI: 10.1016/S0140-6736 (20)30628-0]

69 **World Health Organization**. WHO interim guidance on the clinical management of COVID-19. [cited 10 January 2021]. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>

70 **Shekar K**, Badulak J, Peek G, Boeken U, Dalton HJ, Arora L, Zakhary B, Ramanathan K, Starr J, Akkanti B, Antonini MV, Ogino MT, Raman L, Barret N, Brodie D, Combes A, Lorusso R, MacLaren G, Müller T, Paden M, Pellegrino V; ELSO Guideline Working Group. Extracorporeal Life Support Organization Coronavirus Disease 2019 Interim Guidelines: A Consensus Document from an International Group of Interdisciplinary Extracorporeal Membrane Oxygenation Providers. *ASAIO J* 2020; **66**: 707-721 [PMID: 32604322 DOI: 10.1097/MAT.0000000000001193]

71 **Ramanathan K**, Antognini D, Combes A, Paden M, Zakhary B, Ogino M, MacLaren G, Brodie D, Shekar K. Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases. *Lancet Respir Med* 2020; **8**: 518-526 [PMID: 32203711 DOI: 10.1016/S2213-2600 (20)30121-1]

72 **Falcoz PE**, Monnier A, Puyraveau M, Perrier S, Ludes PO, Olland A, Mertes PM, Schneider F, Helms J, Meziani F. Extracorporeal Membrane Oxygenation for Critically Ill Patients with COVID-19-related Acute Respiratory Distress Syndrome: Worth the Effort? *Am J Respir Crit Care Med* 2020; **202**: 460-463 [PMID: 32543208 DOI: 10.1164/rccm.202004-1370LE]

73 **Barbaro RP**, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, Bartlett RH, Tonna JE, Hyslop R, Fanning JJ, Rycus PT, Hyer SJ, Anders MM, Agerstrand CL, Hryniewicz K, Diaz R, Lorusso R, Combes A, Brodie D, Extracorporeal Life Support Organization. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. *Lancet* 2020; **396**: 1071–1078. [PMID: 32987008 DOI: 10.1016/S0140-6736(20)32008-0]

74 **ELSO**. Full COVID-19 Registry Dashboard. [cited 10 January 202]. Available from: <https://www.elso.org/Registry/FullCOVID19RegistryDashboard.aspx>

75 **Bartlett RH**, Ogino MT, Brodie D, McMullan DM, Lorusso R, MacLaren G, Stead CM, Rycus P, Fraser JF, Belohlavek J, Salazar L, Mehta Y, Raman L, Paden ML. Initial ELSO Guidance Document: ECMO for COVID-19 Patients with Severe Cardiopulmonary Failure. *ASAIO J* 2020; **66**: 472-474 [PMID: 32243267 DOI: 10.1097/MAT.0000000000001173]

76 **Rajagopal K**, Keller SP, Akkanti B, Bime C, Loyalka P, Cheema FH, Zwischenberger JB, El Banayosy A, Pappalardo F, Slaughter MS, Slepian MJ. Advanced Pulmonary and Cardiac Support of COVID-19 Patients: Emerging Recommendations From ASAIO*-*a Living Working Document. *Circ Heart Fail* 2020; **13**: e007175 [PMID: 32357074 DOI: 10.1161/CIRCHEARTFAILURE.120.007175]

77 **Valchanov K**, Krishnan U, Hoole SP, Davies WR, Pettit S, Jones N, Parmar J, Catarino P, Osman M, Berman M. COVID-19 patient with coronary thrombosis supported with ECMO and Impella 5.0 ventricular assist device: a case report. *Eur Heart J Case Rep* 2020; **4**: 1-6 [PMID: 33442588 DOI: 10.1093/ehjcr/ytaa342]

78 **Hodges K**, Mubashir M, Insler J, Estep J, Hsich E, Tong M, Insler S, Soltesz E. Successful management of COVID-19 and associated coagulopathy in a patient with durable left ventricular assist device. *J Card Surg* 2020; **35**: 3202-3204 [PMID: 32789890 DOI: 10.1111/jocs.14937]

79 **Chau VQ**, Oliveros E, Mahmood K, Singhvi A, Lala A, Moss N, Gidwani U, Mancini DM, Pinney SP, Parikh A. The Imperfect Cytokine Storm: Severe COVID-19 With ARDS in a Patient on Durable LVAD Support. *JACC Case Rep* 2020; **2**: 1315-1320 [PMID: 32292915 DOI: 10.1016/j.jaccas.2020.04.001]

80 **Singh R**, Domenico C, Rao SD, Urgo K, Prenner SB, Wald JW, Atluri P, Birati EY. Novel Coronavirus Disease 2019 in a Patient on Durable Left Ventricular Assist Device Support. *J Card Fail* 2020; **26**: 438-439 [PMID: 32305569 DOI: 10.1016/j.cardfail.2020.04.007]

81 **Korada SKC**, Mann JA, Hasan AK, Baliga RR, Mokadam NA, Benza RL, Vallakati A. Management of COVID-19 in a durable left ventricular assist device recipient: A continuity of care perspective. *Heart Lung* 2020; **49**: 688-691 [PMID: 32861886 DOI: 10.1016/j.hrtlng.2020.08.012]

82 **Sobol I**, Yuzefpolskaya M, Roth Z, Colombo PC, Horn E, Takeda K, Sayer G, Uriel N, Naka Y. Characteristics and Outcomes of Patients With a Left Ventricular Assist Device With Coronavirus Disease-19. *J Card Fail* 2020; **26**: 895-897 [PMID: 32956813 DOI: 10.1016/j.cardfail.2020.09.011]

83 **Feldman D**, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, El-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaan A, Kusne S, Loebe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J; International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant* 2013; **32**: 157-187 [PMID: 23352391 DOI: 10.1016/j.healun.2012.09.013]

84 **Carda S**, Invernizzi M, Bavikatte G, Bensmaïl D, Bianchi F, Deltombe T, Draulans N, Esquenazi A, Francisco GE, Gross R, Jacinto LJ, Moraleda Pérez S, O'dell MW, Reebye R, Verduzco-Gutierrez M, Wissel J, Molteni F. COVID-19 pandemic. What should Physical and Rehabilitation Medicine specialists do? A clinician's perspective. *Eur J Phys Rehabil Med* 2020; **56**: 515-524 [PMID: 32434314 DOI: 10.23736/S1973-9087.20.06317-0]

85 **Lal A**, Mishra AK, John K, Akhtar J. Corticosteroids and rehabilitation in COVID-19 survivors. *J Formos Med Assoc* 2021; **120**: 1284-1285 [PMID: 33341350 DOI: 10.1016/j.jfma.2020.12.005]

86 **Smith JM**, Lee AC, Zeleznik H, Coffey Scott JP, Fatima A, Needham DM, Ohtake PJ. Home and Community-Based Physical Therapist Management of Adults With Post-Intensive Care Syndrome. *Phys Ther* 2020; **100**: 1062-1073 [PMID: 32280993 DOI: 10.1093/ptj/pzaa059]

87 **Long L**, Mordi IR, Bridges C, Sagar VA, Davies EJ, Coats AJ, Dalal H, Rees K, Singh SJ, Taylor RS. Exercise-based cardiac rehabilitation for adults with heart failure. *Cochrane Database Syst Rev* 2019; **1**: CD003331 [PMID: 30695817 DOI: 10.1002/14651858.CD003331.pub5]

88 **Schmidt C**, Magalhães S, Barreira A, Ribeiro F, Fernandes P, Santos M. Cardiac rehabilitation programs for heart failure patients in the time of COVID-19. *Rev Port Cardiol (Engl Ed)* 2020; **39**: 365-366 [PMID: 32680654 DOI: 10.1016/j.repc.2020.06.012]

89 **D'Amario D**, Restivo A, Canonico F, Rodolico D, Mattia G, Francesco B, Vergallo R, Trani C, Aspromonte N, Crea F. Experience of remote cardiac care during the COVID-19 pandemic: the V-LAP™ device in advanced heart failure. *Eur J Heart Fail* 2020; **22**: 1050-1052 [PMID: 32431021 DOI: 10.1002/ejhf.1900]

90 **Mitter SS**, Alvarez-Garcia J, Miller MA, Moss N, Lala A. Insights From HeartLogic Multisensor Monitoring During the COVID-19 Pandemic in New York City. *JACC Heart Fail* 2020; **8**: 1053-1055 [PMID: 33272384 DOI: 10.1016/j.jchf.2020.09.009]

**Footnotes**

**Conflict-of-interest statement:** Authors claim no conflicts of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Corresponding Author's Membership in Professional Societies:** Society of Critical Care Medicine; American College of Physicians; American College of Chest Physicians

**Peer-review started:** March 19, 2021

**First decision:** May 5, 2021

**Article in press:** November 25, 2021

**Specialty type:** Virology

**Country/Territory of origin:** United States

**Peer-review report’s scientific quality classification**

Grade A (Excellent): A

Grade B (Very good): B

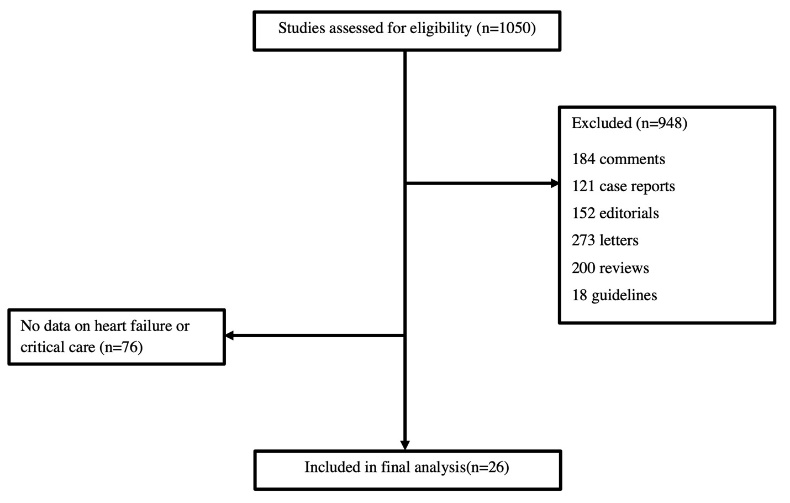
Grade C (Good): C

Grade D (Fair): D

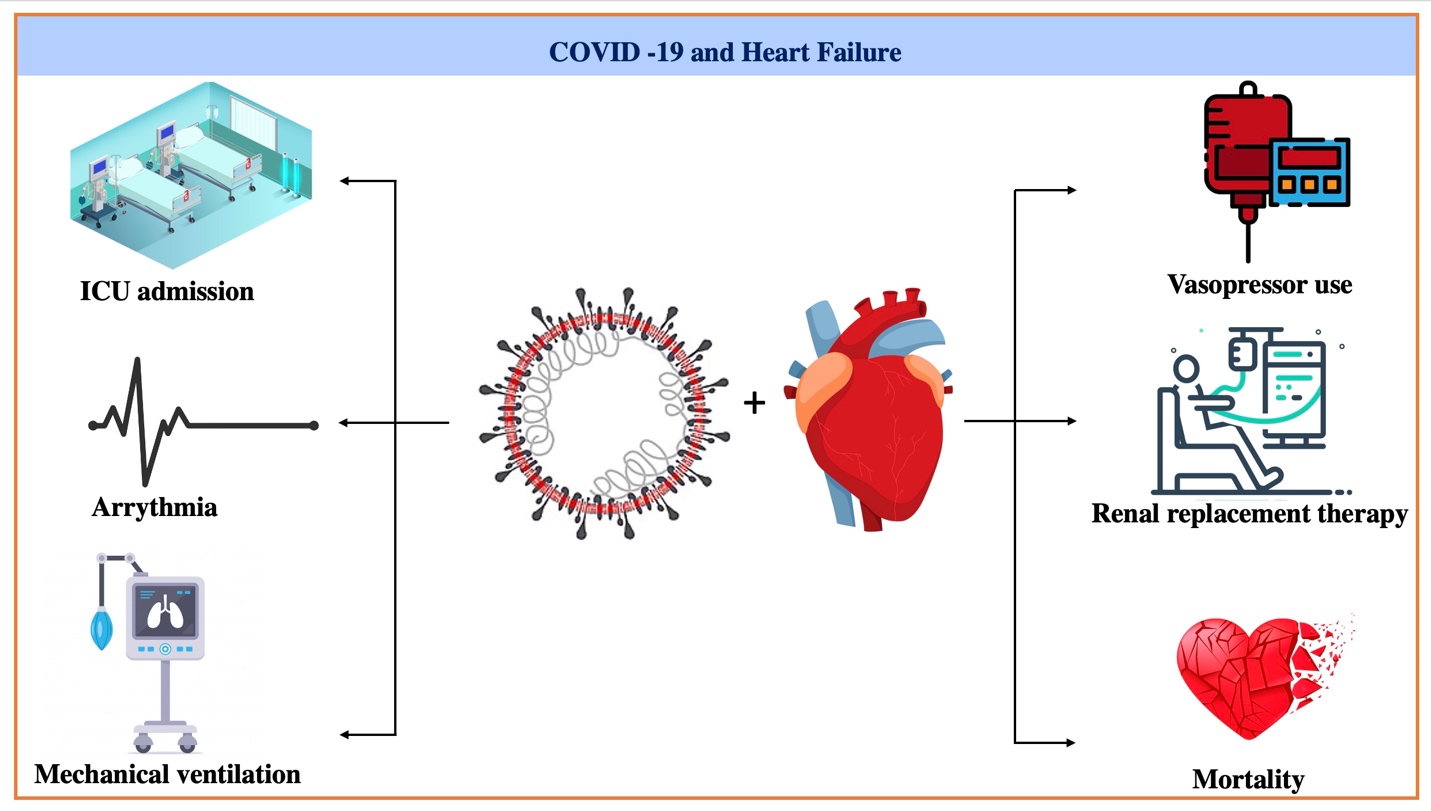
Grade E (Poor): 0

**P-Reviewer:** Barison A, Jha AK, Velikova TV **S-Editor:** Liu M **L-Editor:** A **P-Editor:** Liu M

**Figure Legends**



**Figure 1 CONSORT diagram.**



**Figure 2 Coronavirus disease 2019 and heart failure.**

**Table 1 Studies highlighting prevalence of heart failure, requirement of intensive care unit level of care and outcomes in hospitalized coronavirus disease 2019 patients, *n* (%)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No.** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** |
| Ref. | Inciardi *et al*[1] | Singer *et al*[2] | Zylla *et al*[3] | Russo *et al*[4] | Bhatla *et al*[5] | Peltzer *et al*[6] | Lala *et al*[7] | Shi *et al*[8] | Zhou *et al*[9] | Chen *et al*[10] | Jarrett *et al*[11] |
| Country | Italy | United States | Germany | Italy | United States | United States | United States | China | China | China | United States |
| Total number of patients | 99 | 737 | 166 | 414 | 700 | 1053 | 2736 | 416 | 191 | 274 | 2634 (all patients died) |
| Patients with  chronic heart failure | 21 (21) | 39 (5) | - | 46 (11.1) | 88 (13) | 79 (7.5) | 276 (10.1) | 17 (4.1) | - | 1 (< 1) | 291 (11.1) |
| Newly diagnosed  LV dysfunction | - | - | 5 (3) | - | - | - | - | - | 44 (23) | 43/176 (24) | - |
| Study type | RC, single centre | RC, single centre | RC,  multicenter | RC, multicenter | RC, single centre | RC, multicenter | RC, multicenter | RC, single centre | RC, multicenter | RC, single center | RC of in-patients who died of COVID-19 in a single center |
| Age (mean ± SD) | 67 ± 12 | 60 ± 18 | 64.1 ± 16.7 | 66.9 ± 15.0 | 50 ± 18 | 62 ± 17 | 66.4 (median) | 64 (range: 21-95) | 56 (IQR: 46-67) | 62 (IQR: 44-70) | Range: 21-107 |
| Male | 8 (81) | 423 (57) | 108 (65.1) | 253 (61.1) | 315 (45) | 653 (62) | 1630 (59.5) | 205 (49.3) | 119 (62) | 171 (62) | 1664 (63.2) |
| LVEF, % (mean ± SD) | 48 ± 14 | - | 53.0 ± 12.3 | - | - | HFrEF: 41 (3.8) | - | - | - | - | - |
| ICU admission | 12 (12) | 59 (8) | 65 (39.2) | - | 79 (11.28) | 349 (33.14) | - | - | 50 (26) | - | 1299 (49.3) |
| NIV | 18 (19.1) | 40 (5) | 39 (23.5) | - | - | - | - | 32 (7.7) | 26 (14) | 102 (37) | - |
| IV | 2 (2) | 149 (20.2) | 37 (22.3) | - | - | 327 (31.05) | 307 (11.2) | 51 (12.3) | 32 (17) | 17 (6) | 140 (53.2) |
| ECMO/ICD/CRT/PPM | - | - | PPM:3 (1.8), ICD:2 (1.2), ECMO:3 (1.8) | - | - | - | - | - | ECMO: 3 (2) | ECMO: 1 (<m1) | - |
| Vasopressor | - | - | 30 (18.1) | - | - | 323 (30.67) | - | - | - | - | - |
| Hospital LOS, d, (mean ± SD) | 11.4 ± 6.5 | 4.7 ± 3.0 | 10.5 (IQR 5-22 d)  [ICU stay: 8 (IQR 4-22.5)] | - | - | - | 5.75 (IQR :3.36-9.56) | - | 11 (7–14) [ICU stay: 8 (4–12)] | - | - |
| Complications | Venous thrombo-embolism: 12 (12), Arterial thrombo-embolism: 3 (3), septic shock/sepsis: 6 (6) | - | - | - | - | Bacteremia:  100 (9.5), VTE: 54 (5.13), stroke/TIA:  18 (1.71), AKI requiring RRT: 34 (3.23) | Hospitalized at time of  study publication: 1098 (40.1) | CRRT: 2 (0.5), ARDS: 97 (23.3), Coagulation disorders: 12 (2.9), hospitalized at end of study period:319 (76.7) | RRT: 10 (5), sepsis:112 (59), respiratory failure: 103 (54), ARDS: 59 (31), septic shock: 38 (20), coagulopathy: 37 (19), secondary infection:28 (15) | AKI: 29 (11),CRRT: 3 (1), sepsis: 179 (65), DIC: 21 (8), shock: 46 (17), ALI: 13 (5) | - |
| Mortality | 26 (26) | 68 (9) | 26 (15.7) | 107 (25.8) | 30 (4) | 184 (17.47) | 506 (18.5) | 57 (13.7) | 54 (28.2) | 113 (40) | 2634 (100) |

- Signifies that the variable was not reported in the study.

LV: Left ventricle; RC: Retrospective cohort; LVEF: Left ventricle ejection fraction; HFrEF: Heart failure with reduced ejection fraction; ICU: Intensive care unit; NIV: Non-invasive ventilation; IV: Invasive ventilation; ECMO: Extra-corporeal membrane oxygenation; ICD: Implantable cardiovascular-defibrillator; CRT: Cardiac resynchronisation therapy; PPM: Permanent pacemaker; LOS: Length of stay; IQR: Inter-quartile range; VTE: Venous thrombo-embolism; TIA: Transient ischemic attack; AKI: Acute kidney injury; CRRT: Continuous renal replacement therapy; RRT: Renal replacement therapy; ARDS: Acute respiratory distress syndrome; ALI: Acute liver injury; DIC: Disseminated intravascular coagulation.

**Table 2 Studies reporting outcomes in coronavirus disease 2019 patients admitted to intensive care unit, *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No.** | **1** | **2** | **3** | **4** | **5** | **6** |
| Ref. | Zeng *et al*[16] | Petrilli *et al*[17] | Bhatla *et al* [5] | Hayek *et al*[18] | Iaccarino *et al*[19] | Arentz *et al*[20] |
| Country | China | United States | United States | United States | Italy | United States |
| Total number of patients in ICU | 35 | 990 | 79 | 5019 | 395 | 21 |
| Patients with chronic heart failure | NR | 189 (19.1) | 22 (28) | 512 (10.20) | 60 (15.2) | 9 (42.9) |
| Newly diagnosed LV dysfunction/acute heart failure | 5 (14) | - | - | 166 (3.3) | - | 7 (33.3) |
| Study type | Retrospective cohort, single centre | Prospective cohort, single centre | Retrospective cohort, single centre | Retrospective cohort, multicenter | Cross-sectional study, multicenter | Retrospective cohort, single centre |
| Age, (mean ± SD) | 64.00 (59.50–68.00) | 68 (58-78) | 63 ± 16 | 60 ± 15, 63 ± 141 | 68.9±0.7 | 70 (43-92) range |
| Male | 23 (66) | 656 (66.3) | 40 (51) | 3165 (63.06) | 291 (73.7) | 11 (52) |
| Risk factors | Hypertension: 13 (37), coronary artery disease: 2 (6), arrhythmia: 2 (6), valvular disease:1 (3), diabetes: 10 (29), COPD: 1 (3) | Diabetes: 389 (39.3), asthma or COPD: 169 (17.1), chronic kidney disease: 259 (26.2), cancer: 138 (13.9) | Coronary heart disease: 21 (27), diabetes mellitus :35 (44), hypertension: 62 (78), atrial fibrillation history: 5 (6), obstructive sleep apnea: 23 (29), COPD: 14 (18), liver disease: 14 (18), chronic kidney disease: 16 (20), current tobacco: 4 (5) | Current or former tobacco use: 2174 (43.31), diabetes mellitus: 2110 (42.04), hypertension:3086 (61.48), coronary artery disease:676 (13.46), chronic obstructive pulmonary disease: 43 (0.85), chronic or end stage kidney disease: 819 (16.31), active malignancy:227 (4.52) | Hypertension: 256 (65.3), obesity: 49 (12.4), diabetes: 90 (22.8), COPD: 41 (10.4), CKD: 34 (8.6), coronary artery disease: 62 (15.7) | Asthma: 2 (9.1), chronic obstructive pulmonary disease: 7 (33.3), diabetes: 7 (33.3), obstructive sleep apnea: 6 (28.6), chronic kidney disease: 10 (47.6), end-stage kidney disease: 2 (9.5), history of solid organ transplant: 2 (9.5), cirrhosis: 1 (4.8), immunosuppression: 3 (14.3) |
| HFrEF, | 5 (14) | - | - | - | - | - |
| HFpEF | 0 (0) | - | - | - | - | - |
| Drugs | - | - | - | - | ACE-inhibitors: 97 (24.6), ARB: 66 (16.7), beta-blockers: 96 (24.3), ca-antagonists: 31 (7.8), diuretics: 58 (14.7), alpha-blockers: 7 (1.8) | - |
| ICD | - | - | 5 (6) | - | - | - |
| Ventilation | 35 (100) | 647 (65.35) | - | - | - | 19 (90.5) |
| NIV | 17 (49) | - | - | - | - | 4 (19) |
| IV | 18 (51) | 647 (65.35) | - | 3663 (72.98) | - | 15 (71) |
| ECMO | 5 (15) | - | - | 176 (3.51) | - | - |
| Vasopressor | NR | - | - | 1617 (32.22) | - | 14 (67) |
| ICU stay duration in days | 38 (33–47) | 36 (32-40) | - | 17 (9-30), 6 (4-10)1 | - | - |
| Organ dysfunction | NR | - | - | Acute kidney injury requiring RRT: 1003 | - | AKI: 4 (19.1), ALI: 3 (14.3) |
| Morbidity | acute cardiac injury: 21 (60), atrial or ventricular tachyarrhythmia:3 (9) | 86 (8.68) patients being ventilated and 74 (7.47) patients still admitted at the end of study period | - | Still in hospital 30 days after ICU admission: 169 | - | Admitted in ICU at end of study: 8 (38.1) |
| Mortality | 3 (9) | 485 (49) | - | 2043 (40.71) | - | 11 (52.4) |

1Baseline characteristics of patients who did not have cardiac arrest and those who had cardiac arrest respectively.

- Signifies that the variable was not reported in the study.

ICU: Intensive care unit; LV: Left ventricle; COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; HFrEF: Heart failure with reduced ejection fraction; HFpEF: Heart failure with preserved ejection fraction; ACE: Angiotensin converting enzyme; ARB: Angiotensin receptor blocker; ICD: Implantable cardiovascular-defibrillator; NIV: Non-invasive ventilation; IV: Invasive ventilation; ECMO: Extra-corporeal membrane oxygenation; ECMO: Extra-corporeal membrane oxygenation; RRT: Renal replacement therapy; AKI: Acute kidney injury; ALI: Acute liver injury.

**Table 3 Studies reporting outcomes in heart failure patients with coronavirus disease 2019,** ***n* (%)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **1** | **2** | **3** | **4** | **5** |
| Ref. | Bhatt *et alI*[21] | Alvarez-Garcia *et al*[22] | Caraballo *et al*[23] | Tomasoni *et al*[24] | Andersson *et al*[25] |
| Country | United States | United States | United States | Italy | Denmark |
| Patient number | 8383 | 422 | 206 | 90 | 90 |
| Study type | Retrospective cohort, multicentre | Retrospective cohort, multicentre | Retrospective cohort, multicentre | Retrospective cohort, multicentre | Retrospective cohort. multicentre |
| Age, (mean±SD) | 71.7 ± 13.2 | 72.5 ± 13.3 | 78 (IQR: 65-87) | 73.0 ± 11.4 |  |
| Male | 4178 (49.8) | 236 (55.9) | 93 (45.1) | 66 (73.3) |  |
| Risk factors | Obesity: 2461 (29.4), morbid obesity: 1425 (17.0), hypertension: 6997 (83.5), diabetes: 5107 (60.9), history of arrhythmia: 4548 (54.3), valvular disease: 1417 (16.9), kidney disease: 5020 (59.9), ESKD: 1689 (20.1), smoking: 3665 (43.7), pulmonary disease: 3539 (42.2), asthma: 628 (7.5), anemia: 628 (7.5), malignancy: 290 (3.5) | Obesity: 169 (40.0), hypertension: 382 (90.5), diabetes mellitus: 269 (63.7), dyslipidemia: 228 (54.0), CAD: 235 (55.7), stroke: 114 (27.0), atrial fibrillation: 160 (37.9), CKD: 177 (41.9), COPD: 94 (22.3), asthma: 58 (13.7), OSA: 57 (13.5) | Hypertension: 164 (79.6)  COPD: 67 (32.5)  CAD: 73 (35.4)  Renal disease:7 9 (38.3) | Smoker: 42 (55.3), hypertension: 68 (75.6), dyslipidaemia: 56 (62.2), diabetes: 37 (41.1), atrial fibrillation: 42 (46.7), coronary artery disease: 55 (61.1), COPD: 22 (24.4), CKD: 49 (54.4) |  |
| LVEF (%), (mean ± SD) | - | - | - | 42.1 ± 13.1 | - |
| HFrEF | 3318 (39.6) | 128 (30.3) | 36 (17.5) | 64 (71) | - |
| HFmrEF | - | 44 (10.4) | - | - | - |
| HFpEF | 3486 (41.6) | 250 (59.3) | - | 26 (29) | - |
| RV dysfunction | - | - | - | 16 (28.6) | - |
| Drugs prior to hospitalization | - | RAAS inhibitors: 260 (61.6), beta-blockers: 354 (83.9), MRA: 60 (14.2), loop diuretics: 318 (75.4), thiazides: 64 (15.2), antiplatelet: 327 (77.5), anticoagulant: 175 (41.5), statins: 351 (83.2) | ACEi/ARB: 58 (28.2), beta-blocker: 94 (45.6), CCB: 69 (33.5), SGLT2i: 1 (0.5), warfarin: 16 (7.8), NOAC: 47 (22.8), diuretic: 99 (48.1), statin: 117 (56.8) | ACEi/ARBs/ARNI: 42 (50.0), MRAs: 23 (34.8), beta-blockers: 69 (81.2), direct oral anticoagulants: 17 (20.5), warfarin: 18 (21.6), statins: 47 (56.0) | - |
| ICD/CRT | - | - | - | ICD: 20 (22.2), CRT: 8 (8.9) (both prior to hospitalization) | - |
| ICU | 2431 (29) | 98 (23.2) | - | - | - |
| Ventilation | - | 96 (22.8) | - | - | - |
| NIV | - | - | - | 28 (31.1) | - |
| IV | - | 96 (22.8) | - | 5 (5.6) | - |
| ECMO | 3 (0.04) | - | - | - | - |
| ICU stay duration | - | 5 (2-11) | - | - | - |
| Mortality | 2026 (24.2) | 169 (40.0) | 41 (20) | 37 (41.1) | 33 (27) |

- Signifies that the variable was not reported in the study.

ESKD: End stage kidney disease; CAD: Coronary artery disease; CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; OSA: Obstructive sleep apnea; LVEF: Left ventricle ejection fraction; HFrEF: Heart failure with reduced ejection fraction; HFmrEF: Heart failure with mid-range ejection fraction; HFpEF: Heart failure with preserved ejection fraction; RV: Right ventricle; RAAS: Renin angiotensin aldosterone system; MRA: Mineralocorticoid receptor antagonist; ACEi: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker; SGLT: Sodium-glucose linked transporter; NOAC: Novel oral anticoagulants; ARNI: Angiotensin receptor II blocker – neprilysin inhibitor; ICD: Implantable cardiovascular-defibrillator; CRT: Cardiac resynchronisation therapy; ICU: Intensive care unit; NIV: Non-invasive ventilation; IV: Invasive ventilation; ECMO: Extra-corporeal membrane oxygenation.

**Table 4** **Studies reporting outcomes in heart-transplant patients with coronavirus disease 2019, *n* (%)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **No.** | **1** | **2** | **3** | **4** | **5** |
| Ref. | Latif *et al*[27] | Ketcham *et al*[28] | Singhvi *et al*[29] | Lima *et al*[30] | Bottio *et al*[31] |
| Country | United States | United States | United States | United States | Italy |
| Patient number | 28 | 6 | 22 | 5 | 38 |
| Study type | Retrospective observational | Retrospective observational | Retrospective observational | Retrospective observational | Retrospective observational |
| Age, (mean ± SD) | 64 (53.5-70.5) | 57 (34–73)1 | 58.6 (49.1–71.2)2 | 62 ± 9.8 | 64.9 ± 12.0 |
| Male | 22 (79) | 6 (100) | 14 (63.6) | 4 (80) | 31 (82) |
| Risk factors | Hypertension:20 (71), diabetes:17 (61), lung disease: 10 (36), malignancy: 5 (18), chronic kidney disease: 10 (36) | Chronic heart failure: 4 (67), chronic kidney disease: 4 (67), Chronic anemia: 3 (50), coronary artery disease: 4 (67), former tobacco smoker: 1 (17), diabetes mellitus: 4 (67), hypertension: 6 (100), obesity: 3 (50), obstructive sleep apnea: 3 (50) | Hypertension: 21 (95.5), diabetes: 12 (54.5), lung disease: 3 (13.6), chronic kidney disease stage ≥ III: 14 (63.6), end stage renal disease on dialysis: 3 (13.6), malignancy (excluding non-melanoma skin cancers): 6 (27.3), HIV: 1 (4.5), current smoker: 1 (4.5), former smoker: 7 (31.8), permanent pacemaker: 3 (13.6), charlson comorbidity index ≥ 5: 12 (54.5) | Ischemic cardiomyopathy (pre‐HTx): 2 (40), hypertension: 5 (100), hyperlipidemia: 3 (60), diabetes mellitus: 1 (20), obesity: 2 (40), post‐transplant renal insufficiency: 2 (40) | Obesity: 7 (18), arterial hypertension: 25 (66), dyslipidemia: 18 (47), diabetes mellitus: 7 (18), former smoker: 8 (21), peripheral vascular disease: 8 (21), COPD: 3 (8), stroke: 1 (2), malignancy: 3 (8), previous PCI: 11 (29) |
| NYHA class | - | - | - | - | I:27 (71), II:8 (21), III:3 (8), IV:0 (0) |
| ICU | 7 (25) | 6 (100) | 4 (18.18) | 2 (40) | 4 (10.5) |
| Ventilation | 7 (25) | 5 (83) | 7 (31.81) | 2 (40) | 17 (44) |
| NIV | - | 0 | 3 (13.63) | 0 | 15 (39.4) |
| IV | 7 (25) | 5 (83) | 4 (18.18) | 2 (40) | 2 (5.2) |
| ECMO | - | 0 | - | 0 | 0 (0) |
| Vasopressor | - | 5 (83) | 3 (13.63) | - | 3 (7.9%) |
| ICU stay duration in days | - | 8.25 (4-12.5) | 7 (4-9) | - | - |
| Organ dysfunction | HD: 3 (10.71) | AKI requiring CRRT: 5 (83) | RRT: 3 (13.63) | AKI requiring HD: 1 (20) | - |
| Morbidity | 4 (18) patients remained hospitalized at the end of study period | 2 (33) patients still admitted at the end of the study period | - | One patient developed mild acute cellular rejection | Bacterial coinfection:5 (13), sepsis: 4 (10.5), neurological complication: 1 (2.6), gastrointestinal complication: 1 (2.6) |
| Mortality | 7 (25) | 2 (33) | 4 (18.18) | 0 (0) | 14 (36.8) |

1Range.

2IQR.

- signifies that the variable was not reported in the study. All patients had COVID-19 confirmed by RT-PCR.

HIV: Human immunodeficiency virus; Htx: Heart transplant; PCI: Percutaneous coronary intervention; COPD: Chronic obstructive pulmonary disease; NYHA: New York Heart Association; ICU: Intensive care unit; NIV: Non-invasive ventilation; IV: Invasive ventilation; ECMO: Extra-corporeal membrane oxygenation; HD: Hemodialysis; AKI: Acute kidney injury; CRRT: Continuous renal replacement therapy; RRT: Renal replacement therapy; AKI: Acute kidney injury.



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2022 Baishideng Publishing Group Inc. All rights reserved.**