Clinical presentation of severe COVID-19 with heart failure: A single-center retrospective study

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Abstract. The coronavirus disease-19 (COVID-19) pandemic has led to a global transformation in public health interventions. The present study aimed to evaluate the clinical features as well as the outcomes of severe heart failure (HF) among patients with severe COVID-19. A single-center observational study was carried out at The 904th Hospital of Joint Logistic Support Force (Wuxi, China) from November 2022 to April 2023, and a total of 210 patients diagnosed with severe HF were included. Among these patients, 128 patients had COVID-19 whereas the remaining patients were not diagnosed with COVID-19. The analysis entailed investigated pre-existing medical records, that is, admission and discharge, laboratory values, neuroimaging, length of hospitalization, mortality and costs incurred by patients throughout the COVID-19 pandemic from the records. All the 210 incorporated patients accomplished the follow-up and it was established that there was no significant differences in baseline characteristics between HF combined with COVID-19 and HF without COVID-19 were affirmed (P>0.05). HF coupled with COVID-19 infection demonstrated an increased risk of 30-day mortality (28.91 vs. 14.63%; P=0.017), extended length of hospital stays (22.54±6.73 vs. 19.35±5.69; P<0.001) and higher expenses for hospitalization (P<0.001). Complications related to hospitalization, including pneumonia (76.56 vs. 35.37%; $P=1.0x10^{-4}$), respiratory failure (47.66 vs. 24.39%; P=0.001), pulmonary embolism (8.59 vs. 2.44%; P=0.031), deep vein thrombosis (30.47 vs. 14.63%; P=0.009), 7 days delirium (60.16 vs. 45.12%; P=0.033), multiple organ dysfunction syndrome (32.81 vs. 18.29%; P=0.021) and neurological deficits (30.47% vs. 17.07%, P=0.029) increased significantly. In conclusion, HF combined with COVID-19, treatment and prognosis are getting worse. Enhancing preparedness for future COVID-19 and other similar pandemics necessitates the comprehension of this to refine care provided to patients with HF (registration no. THH-IPR-20221101 on 01 November 2022).

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Introduction

Coronavirus disease-19 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has altered the strategies applied in public health and caused numerous fatalities worldwide (1). For ~3 years it has been evident that the healthcare system has been adversely confronted by the pandemic crisis and this has suppressed the therapeutic management of patients in a global perspective, especially patients managed in the intensive care units (ICUs) (2).

China, characterized by its distinct strategy to counter the outbreak prior to November 2022, employed a series of interventions commencing with the Wuhan lockdown (2020) and executed a dynamic zero-COVID policy. Additionally, the Chinese government employed preventive and control measures to stop the proliferation of SARS-CoV-2, and these measures made them unique in comparison to other nations (3). As deregulation contributed to the COVID-19 outbreak, there are expectations that China makes modifications to its prevention and control strategies by November 2022. The sudden emergence of the SARS-CoV-2 in China adversely impacted the country's healthcare sector, resulting in remarkable disruption and nearly complete breakdown of the medical infrastructure. Despite hospitals admitting a considerable number of patients with COVID-19, few pieces of literature exist on the likelihood of severe illness connected to several comorbidities that present together with COVID-19 (4). In particular, heart failure (HF) combined with COVID-19 infection can escalate into a severe respiratory condition, resulting in a heightened surge in mortality rates (5,6).

Acute heart failure (ACF) is a common clinical severe disease that is characterized by ischemia, hypoxia, dyspnea and other clinical symptoms. Acute pulmonary edema is the main clinical manifestation, which can progress to cardiogenic shock or cardiac arrest and can lead to mortality in severe cases (7). COVID-19 exacerbates HF in patients with preexisting conditions by affecting the cardiovascular system (8). A significant association has been found between COVID-19 and ischemic HF (IHF), contributing to the progression of

the disease and increasing mortality in patients with IHF (9). Bhatt *et al* (10) also reported that patients with cardiovascular disease and HF are more likely to experience complications from COVID-19 compared with patients without cardiovascular disease and HF. In India, it was found that there is no significant difference in outcomes for acute decompensated HF, and length of hospital stay remained unchanged during the COVID-19 pandemic (11). Hraiech *et al* (12) demonstrated that, during the COVID-19 epidemic in France, acute respiratory distress syndrome (ARDS) was more likely to develop in undocumented individuals who entered the neonatal ICU.

Previous studies inferred that infection with SARS-CoV-2 caused COVID-19, and the major clinical feature and cause of mortality is respiratory failure (13-15). Millions of patients globally have experienced acute lung injury secondary to the COVID-19 epidemic, with ~5% of infected patients classified as severe (13). This makes these patients susceptible to complications including ARDS, HF, cytokine storms, respiratory failure, VTE, sepsis, and the rate of mortality is >30% (16). Michalski *et al* (17) also revealed that despite COVID-19 being a multi-system disease, it predominantly damages the lungs where severe cases culminate in ARDS and respiratory failure.

During the SARS-CoV-2 outbreak, there has been a notable absence of literature concerning medical characteristics and epidemiology of HF in China. Therefore, the present study aimed to ascertain how the SARS-CoV-2 pandemic impacted shared risk factors and therapeutic approaches employed for individuals with HF.

Materials and methods

Study design and patients. From November 2022 to April 2023, a single-center observational study was carried out at the 904th Hospital of Joint Logistic Support Force (Wuxi, China). Inclusion criteria incorporated the following: i) Patients diagnosed with HF upon admission by two intensivists; and ii) patients aged 18-90 years. The exclusion criteria were as follows: i) Patients with poor prognosis and low expectation of recovery upon admission; ii) patients who were pregnant; iii) patients with multiple organ dysfunction syndrome (MODS); and iv) All patients who underwent treatments which could affect treatment and prognosis were excluded (such as antiviral treatment, hemodialysis treatment, immunotherapy and anti-tumor treatment before admission). Utilizing their COVID-19 infection status, the patients were classified into HF with COVID-19 compared against HF only, and no significant difference in drug treatment was observed between the two groups.

The present study enrolled 210 individuals with HF who satisfied the aforementioned specifications, including 117 (55.71%) male and 93 (44.29%) female patients. The mean age was 65.18 years (standard deviation, 8.71 years) in the HF with COVID-19 group, and 66.43 years (standard deviation, 9.14 years) in the HF without COVID-19 group. Patient data was collected from The 904th Hospital of Joint Logistic Support Force (Wuxi, China), in patients with HF of all ages (aged 18-90 years). Information depicted in pre-existing medical records was analyzed, focusing on factors that may influence prognosis; for instance, sex, age, BMI, smoking history, drinking history and past medical history. Follow-up was conducted via online channels or telephone communication.

The study procedures were designed and executed to ensure the safety and efficacy profiles among individuals with HF after the outbreak of the SARS-CoV-2 virus. The Clinical Research Ethics Committees at Wuxi Taihu Hospital (Wuxi, China) approved the study protocol (approval no. THH-YXLL-2022-1101).

Follow-up and outcome evaluation. All patients completed 6 months of follow-up and survival information was provided for all the patients. Clinical outcomes, complications, hospital stays and hospitalization costs were evaluated. The incidence of delirium within 7 days was evaluated methods as performed in our previous study (18). Delirium was evaluated for a week from patient admission to hospital, but it was not evaluated if the patient remained in a coma.

Statistical analysis. The student's unpaired t-test was used for normally distributed continuous data (mean ± SD), whereas the χ^2 test or the χ^2 test with continuity correction compared the categorical data. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. Calculations for significant risk ratios or mean differences were performed, with two-sided 95% confidence intervals (CI) and $P<0.05$ was considered to indicate a statistically significant difference. Statistical analyses were performed using the IBM SPSS Statistics version 24 for Windows (IBM Corp.).

Results

Baseline patient characteristics: Overall population. During the study period, a comprehensive assessment was executed on the 210 individuals with HF. RT-PCR was utilized to conduct COVID-19 testing on patients. COVID-19 was present in 128 patients who experienced HF, while the remaining 82 patients had HF but did not have COVID-19 (Fig. 1). COVID-19 was used to separate patients into two groups. The group with COVID-19 infection and the group without COVID-19 had average ages of 65.18±8.71 years (range, 43-85 years) and 66.43±9.14 years (range, 46-88 years), respectively. Moreover, no significant distinctions were present in the baseline characteristics (Table I) when comparing HF combined with COVID-19 infection to those without COVID-19. There was no significant difference in drug treatment between the two groups.

Clinical outcome between the two groups. Patients with HF may be predisposed to an elevated risk of mortality following COVID-19 infection. Therefore the present study evaluated the 30-day mortality rate between the two groups. The rate of mortality within 30 days of patient admission to hospital for the group with HF combined with COVID-19 infection and the group with HF without COVID-19 infection was 28.91% (37 out of 128) and 14.63% (12 out of 82), respectively (Fig. 2). The 30-day mortality rate was significantly increased in the group with COVID-19 infection compared with the group without COVID-19 (P=0.017; Fig. 2). A higher total 30-day mortality was linked to the combination of COVID-19 and HF regarding clinical outcomes.

Table I. Comparison of baseline data at admission.

Characteristic	COVID-19 (n=128)	Non-COVID-19 (n=82)	P-value
Age, years	65.18±8.71	66.43±9.14	0.321
Sex, n (%)			0.845
Male	72 (56.25)	45 (54.88)	
Female	56 (43.75)	37 (45.12)	
BMI, kg/cm^2	23.14±4.88	23.85±5.12	0.314
Heart rate, bpm	87.59±12.33	88.29±12.84	0.693
Respiratory rate, bpm	20.06±4.23	21.02±4.84	0.131
PaO_2, mm Hg	57.15±8.71	56.94±8.67	0.865
$PaCO_2$, mm Hg	80.29±15.47	79.83±14.66	0.830
Blood, pH	7.30±1.63	7.33±1.74	0.899
MAP, mm Hg	134.65±22.37	136.49±24.18	0.574
Admitted BNP, ng/ml	972.35±95.39	987.42±92.71	0.260
Smoking history, n (%)			0.568
Yes	52 (40.63)	37 (45.12)	
No	76 (59.37)	45 (54.88)	
Drinking history, n (%)			0.778
Yes	59 (46.09)	36 (43.90)	
No	69 (53.91)	46 (56.10)	
Living environment, n (%)			0.659
Town	84 (65.63)	51 (62.20)	
Countryside	44 (34.37)	31 (37.80)	
Past medical history, n (%)			
Hypertension	89 (69.53)	53 (64.63)	0.459
Hyperlipidemia	60 (46.88)	39 (47.56)	0.923
Diabetes	45 (35.16)	27 (32.93)	0.740
Respiratory system disease	41 (32.03)	25 (30.49)	0.814
Chronic kidney disease	14 (10.94)	7 (8.54)	0.572
Cerebrovascular disease	33 (25.78)	24 (29.27)	0.579
Etiology of heart failure, n (%)			
Coronary artery disease	72 (56.25)	46 (56.10)	0.983
Dilated cardiomyopathy	21 (16.41)	14 (17.07)	0.899
Valvular heart disease	16 (12.50)	12 (14.63)	0.657
Hypertensive heart disease	11 (8.59)	6 (7.32)	0.741
Congenital heart disease	5 (3.91)	3 (3.66)	>0.999
Myocarditis	3 (2.34)	1 (1.22)	>0.999
Severity of heart failure, n			
< III level	27	19	
III level	46	27	
IV level	55	36	

Data are presented as mean ± SD unless otherwise shown. COVID-19, coronavirus disease-19. BMI, body mass index; MAP, mean arterial pressure; $PaCO_2$, partial pressure of CO_2.

Hospital stays and hospitalization costs. Patients with HF combined with COVID-19 infection had an average length of hospitalization of 22.54±6.73 days. On the other hand, patients without COVID-19 had an average stay of 19.35±5.69 days, inferring a statistically substantial disparity (P<0.001; Fig. 3A). In terms of hospitalization costs, the costs for COVID-19-infected and non-COVID-19-infected patients were 4,100$ and 3,350$, respectively, inferring a significantly increased cost for patients with COVID-19 (P<0.001; Fig. 3B). Therefore, the hospital costs and stays for patients with HF have been substantially elevated due to the COVID-19 infection.

Complications between the two groups. While providing treatment for HF, the present study determined a greater

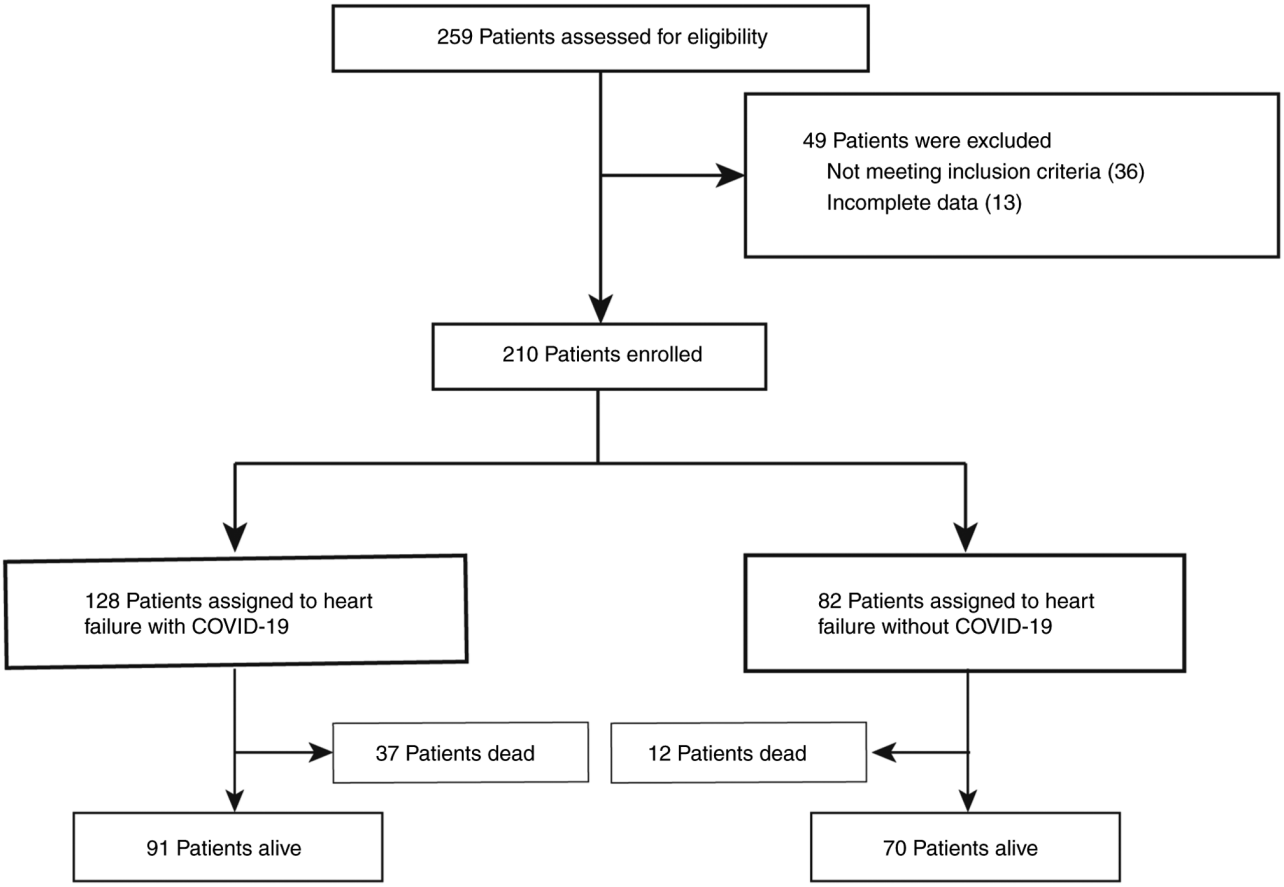

Figure 1. Flow chart of the present study. COVID-19, coronavirus disease-19.

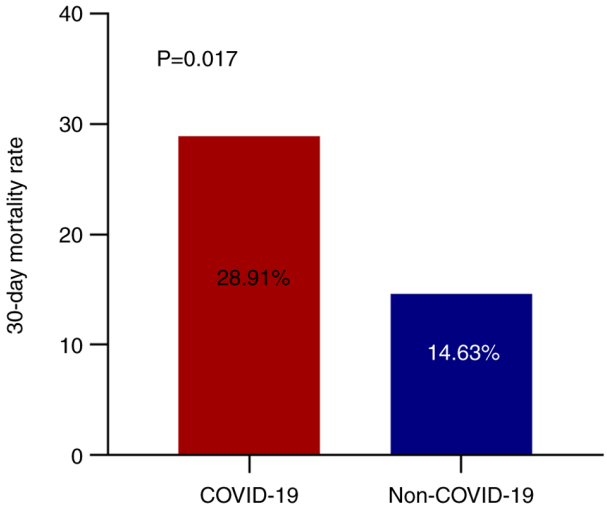

Figure 2. Difference in clinical outcomes between the two groups. COVID-19, coronavirus disease-19.

incidence of complications in patients who were diagnosed with COVID-19. The incidence of pneumonia (76.56 vs. 35.37%; P=1.0x10^{-4}; Table II), respiratory failure (47.66 vs. 24.39%; P=0.001; Table II), pulmonary embolism (8.59 vs. 2.44%; P=0.031; Table II), deep vein thrombosis (DVT; 30.47 vs. 14.63%; P=0.009; Table II), 7 days delirium (60.16 vs. 45.12%; P=0.033; Table II), multiple organ dysfunction syndrome (MODS; 32.81 vs. 18.29%; P=0.021; Table II) and neurological deficits (30.47 vs. 17.07%; P=0.029; Table II) were markedly significantly among COVID-19-infected patients compared with those not infected with COVID-19. The two groups had no substantial disparities in renal failure (21.88 vs. 13.41%; P=0.147), abnormal liver enzymes (41.41 vs. 34.15%; P=0.292), diarrhea (26.56 vs. 18.29%; P=0.167), vomiting (15.63 vs. 10.98%; P=0.341) and electrolyte imbalance (71.88 vs. 64.63%; P=0.268). Table II displays the complications results.

ICU stays and mechanical ventilation. Patients with AHF are critically ill, and most need to be treated in the ICU and receive mechanical ventilation. The present study revealed that the mean length of ICU stays was increased significantly in the patients with HF and COVID-19 group compared with patients without COVID-19 (7.39±2.51 vs. 4.28±2.19, P<0.001; Fig. 4A). Additionally, the present study revealed that the time of mechanical ventilation was longer in the patients with HF and COVID-19 group compared with the patients without COVID-19 (68.77±15.24 vs. 49.28±10.09; P<0.001; Fig. 4B).

Discussion

The present study was executed at a single center and evaluated the impact of the SARS-CoV-2 pandemic on common risk factors and therapeutic management for patients with HF. Between the two groups, the current findings of the present study affirm that no remarkable distinction in the

Table II. Comparison of complications between two groups.

	COVID-19 (n=128)	Non-COVID-19 (n=82)	P-value
Pneumonia, n (%)	98 (76.56)	29 (35.37)	<0.001
Respiratory failure, n (%)	61 (47.66)	20 (24.39)	0.001
Pulmonary embolism, n (%)	11 (8.59)	2 (2.44)	0.031
Deep vein thrombosis, n (%)	39 (30.47)	12 (14.63)	0.009
7 days delirium, n (%)	77 (60.16)	37 (45.12)	0.033
Multiple organ dysfunction syndrome, n (%)	42 (32.81)	15 (18.29)	0.021
Renal failure, n (%)	28 (21.88)	11 (13.41)	0.147
Neurological deficit, n (%)	39 (30.47)	14 (17.07)	0.029
Abnormal liver enzymes, n (%)	53 (41.41)	28 (34.15)	0.292
Diarrhea, n (%)	34 (26.56)	15 (18.29)	0.167
Vomiting, n (%)	20 (15.63)	9 (10.98)	0.341
Electrolyte imbalance	92 (71.88)	53 (64.63)	0.268

COVID-19, coronavirus disease-19.

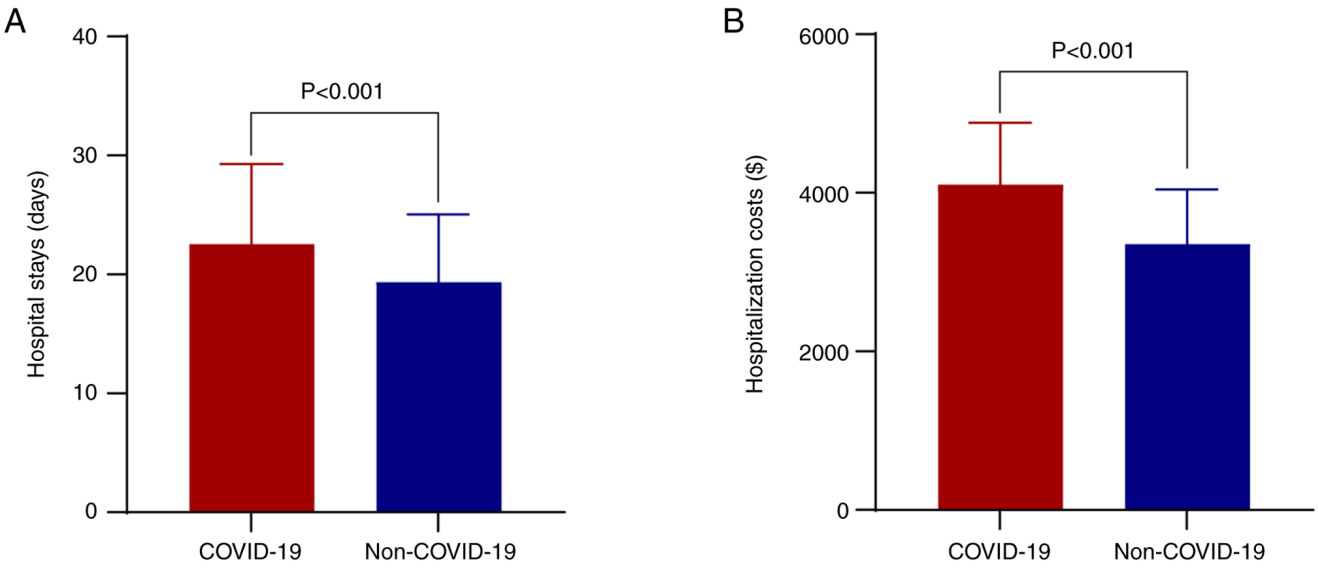

Figure 3. Hospital stays and hospitalization costs. (A) Hospital stays; (B) hospitalization costs. COVID-19, coronavirus disease-19.

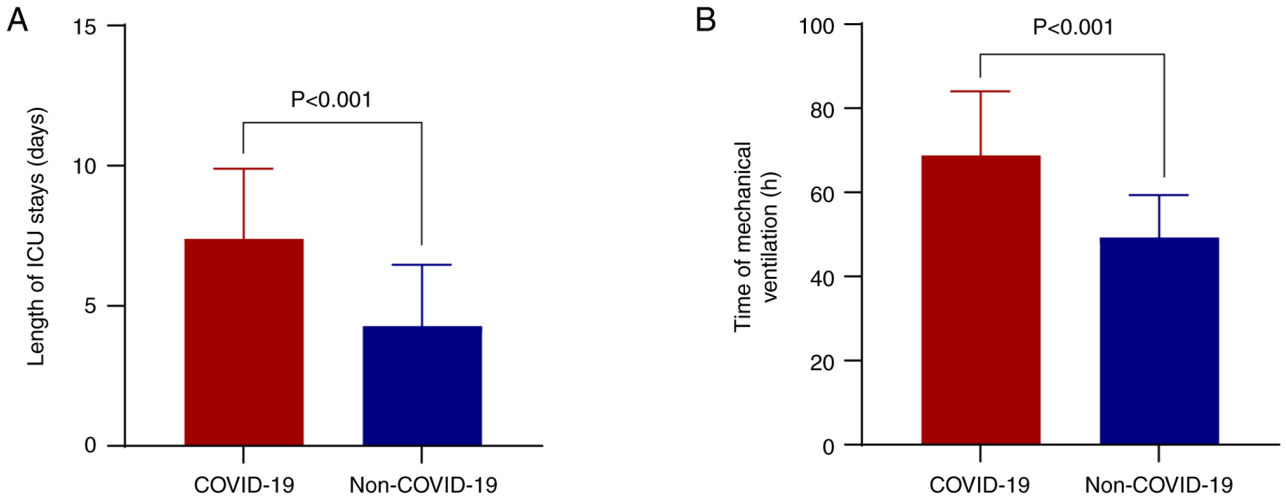

Figure 4. ICU stays and mechanical ventilation. (A) ICU stays; (B) time of mechanical ventilation. ICU, Intensive care unit. COVID-19, coronavirus disease-19.

characteristics of patients on admission. The combination of COVID-19 and HF was linked to an increased in the overall rate of mortality within 30 days. The costs as well as the length of hospital stays were also increased by COVID-19-related HF. COVID-19 along with HF increased the risk of hospitalization complications, including pneumonia, respiratory failure, pulmonary embolism, DVT, delirium, HF, neurological deficits and MODS.

Healthcare systems and practitioners have incurred global repercussions due to the COVID-19 pandemic. Following December 2022, the termination of the zero-COVID strategy led to an escalation in the transmission of COVID-19. A number of patients admitted to the hospital were detected to have contracted COVID-19 before or after admission (4). Overall, there were no discernable disparities in baseline characteristics between HF and COVID-19 infection and those without. The present study ascertained that the concurrence of COVID-19 and HF culminated in worsened clinical results, complications, markedly longer hospital stays and increased costs for patients with HF. In comparison to patients without pulmonary embolism, patients with COVID-19 comorbid with pulmonary embolism exhibit a greater 30-day mortality rate as per Tilliridou *et al* (19). The synergy of COVID-19 infection, multiple traumas and positive CT results elevate the risks of developing pulmonary complications (20). Driessen *et al* (21) demonstrated that the rate of mortality throughout the SARS-CoV-2 pandemic was higher compared with the previous period. In this current investigation, a greater number of patients developed HF infected with COVID-19, and the most common cause of mortality was multiple organ failure from severe lung infections. Moreover, Htay *et al* (22) revealed a significant increase in the rate of mortality among patients with COVID-19 undergoing peritoneal dialysis during the COVID-19 outbreak.

The present study revealed that the total 30-day mortality was higher compared with that in a previous study (11); the main reason for this may be that our hospital is a regional treatment center for critically ill patients, and the patients treated had more serious stages of disease. A high total 30-day mortality was linked to the combination of COVID-19 and HF in the perspective of clinical outcomes in the present study. On the one hand, the COVID-19 pandemic strains medical resources, and when there is a shortage of beds and medicines this results in patients with HF not being able to get effective, rapid treatment. On the other hand, COVID-19 causes many complications in the cardiovascular system and systemic system, which worsens the disease (23). Additionally, the present study also revealed that COVID-19 could lead to more complications. Fatuyi *et al* (24) reported that when acute decompensated HF coexisted with COVID-19 infection this was associated with a higher in-hospital mortality rate. Clinically, patients with HF along with COVID-19 infection need high attention due to higher mortality rates and complications.

To the best of our knowledge, the present study was the first to report the clinical data of HF in patients with COVID-19 infection and explore how the pandemic has impacted the common risk factors and therapeutic approaches for patients with HF. Currently, there is a lack of relevant experience in diagnosis and treatment, the present preliminary results provide a basis for future research on large samples. Additionally, it is not yet clear whether COVID-19 and similar infectious diseases will cause another pandemic again. Therefore, HF along with COVID-19 infection requires high attention.

The present study had two limitations in the study design. Firstly, the sample size was small and this necessitates the conduction of extensive studies in the future to ascertain the impact of the SARS-CoV-2 outbreak on the common risk factors and the therapeutic approaches for individuals with HF. The other limitation is that it is difficult to ascertain a causal relationship utilizing the obtained data because of the nature of our cross-sectional as well as retrospective study. As a result, future research focusing on the impact of COVID-19 on respiratory failure should thus adopt a prospective, longitudinal design. This will facilitate the detection of risk factors in conjunction with the assessment of causal relationships between variables. Moreover, the present study centers on the immediate negative outcomes as well as the effectiveness of COVID-19 infection in patients with HF, stressing the need for long-term findings. Therefore, it is imperative to scrutinize larger and additional groups of patients with HF as a result of COVID-19.

In conclusion, patients with COVID-19 and HF demonstrated heightened mortality rates within 30 days, higher hospitalization expenses, extended hospital stays and a greater possibility of complications occurring during their hospitalization. The results of the present study will provide a reference for future patients with HF along with COVID-19 and need a larger sample study to clarify the long-term prognosis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XL and TL contributed to the conception and design of the study. XL, TL and RW conducted the data collection and the statistical analysis. XL wrote the first draft of the manuscript. RW revised the manuscript, managed the project, coordinated the study and gave final approval for the version to be published. XL, TL and RW confirm the authenticity of all the raw data. All of the authors contributed to manuscript revision and read and approved the final version of the manuscript.

Ethics approval and consent to participate

The registration number THH-IPR-20221101 (date, 01/Nov 2022) was obtained with protocol approval from the Clinical Research Ethics Committees of the Wuxi Taihu Hospital (approval no. THH-YXLL-2022-1101). Prior to enrollment

in the study, all participants (or their legal representatives) provided informed written consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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