



Case Report

# Cardiovascular Complications Associated with Sars-Cov-2 Virus Infection in Critical Ill

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## Abstract

**Introduction:** The COVID-19 pandemic causes more than one million infected worldwide and thousands of deaths. Complications of this disease are in the respiratory system; however, the cardiovascular system is affected with complications including myocardial injury, myocarditis, myocardial infarction, heart failure, arrhythmias and venous thromboembolic episodes.

**Objective:** To determine the cardiovascular complications associated with SARS-CoV-2 virus infection in critical patients.

**Materials and Methods:** A retrospective, observational, transversal, analytical study was carried out, where 133 patients were included in the intensive care unit. Analytical statistics were performed using  $\chi^2$  for the qualitative variables and U Mann-whitney for the quantitative variables of free distribution and t student for those of normal distribution. Multiple logistic regression was performed for the confounding variables.

**Results:** Cardiovascular outcomes such as arrhythmias due to atrial fibrillation, heart failure or coronary thrombosis were associated with heart failure OR 3.1, 95% CI (1.28-7.95), history of treatment with Angiotensin receptor antagonist 2 OR 2.4, 95% CI (1.10-5.30), age over 60 years OR 2.7, 95% CI (1.20-6.20) Troponin I value over 0.205 ng/L OR 2.2, CI95% (1.04-5.37).

**Conclusions:** Patients who had cardiovascular complications the mortality was high.

**Keywords:** COVID-19; Arrhythmias; Heart failure.

## Introduction

The objective of the article is to determine the cardiovascular complications, which are associated with SARS-CoV-2 virus infection in critically ill patients. In December 2019, pneumonia of unknown cause occurred in Wuhan, Hubei Province, China; On January 7, 2020, a new coronavirus, called coronavirus-2 (SARS-CoV-2), was identified. Currently, COVID-19 has spread widely around the world [1]. About 5% of diagnosed cases require critical care to manage serious manifestations and complications. Among COVID-19 patients who are seriously ill, mortality rates of 39% to 72% are reported [2]. Risk factors for a severe course of COVID-19 include people: over the age of 65, living in acyls, obstructive neuropathy (COPD), moderate to severe asthma, serious heart conditions, chemotherapy, history of bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV/AIDS, use of steroids or other immunosuppressive drugs, smoking, BMI Body Mass Index  $\geq 40$  or more, diabetes, Chronic Renal Disease on dialysis and liver disease [3]. One of the risk factors for mortality is cardiovascular disease. The mechanisms by which cause alterations at the myocardial level is that in the renin angiotensin aldosterone axis, angiotensin (Ang) I is converted into Ang II by the effect of the angiotensin-converted enzyme (ACE). Angiotensin II mediates vasoconstrictor, pro-inflammatory and pro-oxidative effects through agonise at the Ang II receptor type 1 (AT 1 R). Angiotensin-converting enzyme 2 converts Ang II into Ang 1-7, which eventually binds to the Mas receptor (MasR) and mediates beneficial actions, including vasodilation and anti-inflammatory, antioxidant and anti-apoptotic effects; Therefore, the ACE2 / Ang 1-7 / MasR axis has opposite actions to the ACE / AngII / AT 1 R [4] axis; that is why ACE2 is widely expressed not only in the lungs but also in the cardiovascular system, in addition to causing a cytokine storm triggered by an unbalanced response by type 1 and type 2 helper T cells and respiratory dysfunction and hypoxemia caused by COVID-19, which damages myocardial cells [5]. Heart injury can result through direct or indirect mechanisms. The direct mechanism involves viral infection in myocardial tissue, resulting in death and inflammation of cardio myocytes. Indirect mechanisms include cardiac stress due to respiratory failure and hypoxemia and cardiac inflammation secondary to severe systemic hyperactive inflammation. Biomarkers (cardiac troponin I and brain-type natriuretic peptide), arrhythmias, myocardial infarction and heart failure are manifestations of myocardial injury [6]. Acute heart injury, defined as a significant elevation of cardiac troponins, is the most commonly reported cardiac abnormality in COVID-19. It occurs in about 8-12% of all patients. Direct myocardial injury due to viral involvement of cardio myocytes and the effect of systemic inflammation appear to be the most common mechanisms responsible for cardiac injury [7]. It is currently unknown whether

heart failure is due to new cardiomyopathy versus an exacerbation of previously undiagnosed heart failure [8]. Importantly, right heart failure can also occur, especially in people with Respiratory Distress Syndrome and acute lung injury in the context of COVID 19 patients in the ICU [9]. Some rhythm disorders can occur against the background of a viral illness due to hypoxia, inflammatory stress, and abnormal metabolism [10]. Patients with COVID-19 are also at increased risk of thromboembolic events, which are due to systemic inflammation, abnormal clotting status, multi-organ dysfunction, and critical illness [11].

## Material and Methods

An observational, analytical, retrospective and transversal study was carried out, where a sample of 135 patients was obtained, which was confirmed by means of a difference in proportions with a power of 80%, a case: control ratio of 1:3, an OR of 4, and an event difference of 30% between the group of cases and controls (50% vs 20%), thus a size of 34 cases with 101 controls is obtained. The inclusion criteria were patients over 18 years of age, men or women who had symptoms of COVID-19, who were admitted to the intensive care area during the period from 2020 to 2021. We excluded 2 patients who had incomplete information. Patients admitted to the intensive care unit were determinate different studies including blood biometry, procalcitonin, D-dimer, ferritin, Troponins, CK, CK MB, reactive protein c , serum electrolytes as well as electrocardiogram and focused cardiac ultrasound. This study was submitted to the Hospital's Local Health Research Committee, which obtained registration number R-2021-1401-033.

## Results

Patients admitted to the intensive care unit were 71.4% male, with a median age of 63 years (IQR 51.5 – 74.5 years). The patients' history was divided into three groups: previous diseases and comorbidities, habits, and previous drug use. Among the comorbidities considered in the present study, obesity was the most important (56.4%), followed by Arterial Hypertension (52.6%), and Diabetes Mellitus (44.4%). On the other hand, among the consumption habits considered in the study, 27.1% of the patients (36 subjects) had tobacco use, while 12.8% of the patients presented alcoholism. Previous pharmacological treatment was also considered, due to previous medical indications for comorbidity. Among them, the consumption of angiotensin receptor antagonists type 2 (47.4%), the consumption of oral hypoglycemic drugs (42.1%), and the consumption of Acetylsalicylic Acid (17.3%) stand out. Among the hemodynamic findings, the calculation of cardiac output and cardiac index by Fick's method was considered, which found a median Cardiac Output 7.3 (RIQ 5.1-10) l/min and a Cardiac Index 3.8 (RIQ 2.7- 5.2) l/min/m<sup>2</sup>. Laboratories include D-dimer 2200 ng/ml (RIQ 1140 - 4550), D-lactic shydrogenase

DHL 463.01 IU/L (RIQ 359.4 - 635.9), IL6 241.55 pg/ml (RIQ 131.86 - 257.62), C-reactive protein 177.8 mg/dl (RIQ 103.3 - 268.9). For the severity of the disease by tomography, the Co RADS score was obtained, which was presented in 5 (RIQ 4-5) Table 1. The main cardiovascular complications in patients with SARS COV-2 infection, the most frequent in the study group were heart failure 16 (12%), and atrial fibrillation 11 (8.3%). The total cardiovascular complications in the population were 53 patients (39.2%) Table 2. The characteristics most frequently associated with cardiovascular outcome is in patients with SARS COV-2 infection, we find the history of heart failure (OR 3.1, 95% CI 1.28-7.95 p 0.02) and the history of treatment with ARA2 (OR 2.4, 95% CI 1.10-5.30, p 0.03), age > 60 years (OR 2.8 95% CI 1.26-6.38 p 0.01) Table 3. The characteristics of the patients associated with mortality, a statistical association of cardiovascular outcomes was found with the variables of age greater than 60 years (OR 2.8 95% CI 1.26-6.38 p 0.01) at the time of admission to the ICU, history of Systemic Arterial Hypertension (OR 3.3, 95% CI 1.62-6.79, p 0.001), history of Chronic Obstructive Pulmonary Disease (OR 3.3, 95% CI 1.36-8.03, p 0.006), history of Heart Failure (OR 25.2 95% CI 3.28-193.33 p <0.001), lactate greater than 2.5 mmol/L (OR 2.8 95% CI 1.11-7.23 p 0.02), Pro-BNP greater than 150 pg/ml (OR 2.4 95% CI 2.4-5.25, p 0.01) Table 4. When adjusting these variables, both Heart Failure (OR 15.81, 95% CI 2.00-124.91, p 0.009) and age over 60 years (OR 3.9, IC 95% 1.42-6.71, p 0.004) Do not lose their significance Graphic 1.

Characteristics	N=133
Age	63 (51.5-74. 5)*
Male	95 (71.4) †
Diabetes mellitus	59 (44.4) †
Arterial Hypertension	70 (52.6) †
COPD	34 (25.6) †
Heart failure	24 (18) †
Obesity	75 (56.4) †
Coronary Heart Disease	23 (17.3) †
Smoking	36 (27.1) †
Stroke on admission	11 (8.3) †
Angiotensin-converting enzyme inhibitors	4 (3) †

Angiotensin II receptor blockers	63 (47.4) †
Lymphocytes (%)	0.53 (0.39-0. 69)*
Platelets (10*3/uL)	210 (162-259) *
D-dimer (ng/ml).	2200 (1140-4550) *
Fibrinogen (mg/dl)	636.5 (578-740. 2)*
C-reactive protein (mg/dl)	177.8 (103.3-268. 9)*
Procalcitonin (ng/dl)	0.35 (0.183-1. 08)*
Lactate Dehydrogenase (UI/L)	463.01 (359.4-635. 9)*
Troponin I (ng/mL)	0.2 (0.1-0. 6)*
BNP (pg/mL)	84.1 (52.9-251. 3)*
Creatina quinasa MB (mg/L)	31.7 (21.4-61. 6)*
Glucose (mg/dl)	160 (117-231) *
Cholesterol (mEq/mL)	130.9 (118.1-155. 2)*
Triglycerides (mEq/mL)	185 (142.4-254. 3)*
Leukocytes (10*3/uL)	11.1 ±5.7++
Interleukin-6 (pg/ml)	241.55 (131.86 – 257.62) *
SvO2 (%)	70 (62-75) *
EB mmol/L	-1.2 (-4.9-1. 6)*
Lactate mmol/L	1.7 (1.3-2. 4)*
VO2 ml	238.7 ±30.3++
Cardiac Output l/min	7.3 (5.1-10) *
Cardiac Index l/min/m2	3.8 (2.7-5. 2)*
CO-RADS	5 (4-5) *
Days of stay in ICU	15 (11-20) *
Admission-discharge days (hospitalization)	16 (12-21) *

† Variables that are represented in frequencies and percentages \* Variables of non-normal distribution that are represented as median and interquartile ranges (RIQ) ++ Normal distribution variables represented in mean and standard deviation (DS). COPD: Chronic Obstructive Pulmonary Disease; BNP: Pro-brain natriuretic peptide; SvO2: Venous oxygen saturation; VO2 oxygen consumption rate; ICU: Intensive Care Unit; CO-RADS: Reporting and Data System for COVID-19.

**Table1:** Baseline characteristics of patients admitted to ICU.

Complications	N=135(%)
Pericarditis	4 (3%)
Dilation of the Right Ventricle	5 (3.8%)
Acute Myocardial Infarction	2 (1.5%)
Ventricular tachycardia	7 (5.3%)
Atrial Fibrillation	11 (8.3%)
Ventricular Fibrillation	1 (0.8%)
Long QT interval	5 (3.8%)
Heart Failure	16 (12%)
Pulmonary embolism	2 (1.5%)

**Table 2:** Cardiovascular complications associated with SARS-CoV-2 virus infection.

Variables	OR	p	Adjusted	
			OR	p
Male	1.2 (0.53-2.77)	Ns		
Diabetes mellitus	1.8 (0.85-3.89)	Ns		
High blood pressure	1.8 (0.84-3.95)	Ns		
COPD	2.1 (0.96-4.98)	Ns		
Heart failure	3.1 (1.28-7.95)	0.02*		
Obesity	1.2 (0.58-2.72)	Ns		
Rheumatic Disease	0.42 (0.08-2.01)		0.34	
Smoking	1.6 (0.71-3.68)	Ns		
IECA	0.8 (0.08-8.22)	Ns		
ARA II	2.4 (1.10-5.30)	0.03*		
Oral antidiabetics	1.8 (0.85-3.89)	Ns		
Hydroxychloroquine	1.1 (0.51-2.42)	Ns		
Azithromycin	1.2 (0.50-2.90)	Ns		
Mechanical ventilation	3.37 (0.73-15.53)	Ns		
Age > 60 years	2.8 (1.26-6.38)	0.01*	2.7 (1.20-6.20)	0.017
PEEP > 10cmH2O	1.1(0.55-2.56)	Ns		
Lactate > 2.5mmol	1.5 (0.63-3.70)	Ns		
Troponin I > 0.205 ng/mL	2.4 (1.11-5.19)	0.02*	2.2 (1.04-5.37)	0.039
SO <sub>2v</sub> %	1.2 (0.59-2.68)	Ns		
VO <sub>2</sub> < 250ml	1.0 (0.46-2.35)	Ns		
BNP> 150 pg/mL	1.2 (0.59-2.79)	Ns		
PaO <sub>2</sub> /FIO <sub>2</sub> <100	1.3 (0.48-3.64)	Ns		

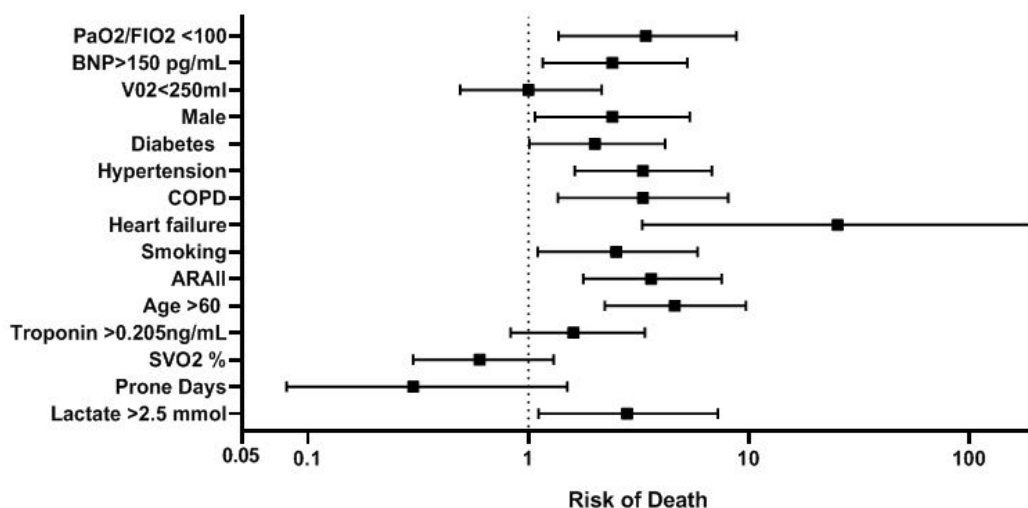
\*Variables with statistical significance p< 0.05 ACE inhibitors: Angiotensin-Converting Enzyme Inhibitors; ARA 2: Angiotensin receptor antagonist 2; COPD: Chronic Obstructive Pulmonary Disease; PEEP: Positive Pressure at the End of Expiration; SVO<sub>2</sub>: Central venous oxygen saturation; VO<sub>2</sub>: Oxygen Consumption; BNP: Brain Natriuretic Peptide. IECA: Angiotensin-converting enzyme inhibitors; ARA II: Angiotensin II receptor blockers.

**Table 3:** Characteristics associated with cardiovascular complications in patients with SARS-CoV-2 virus infection.

Variables	OR	p	Adjusted	
			OR	p
Male	2.4 (1.07-5.39)	0.03*		
Diabetes mellitus	2.0 (1.01-4.16)	0.04*		
Arterial Hypertension	3.3 (1.62-6.79)	0.001*		
COPD	3.3 (1.36-8.03)	0.006*		
Heart failure	25.2(3.28-193.33)	< 0.001*	15.81 (2.00-124.91)	0.009
Smoking	2.5 (1.10-5.84)	0.02*		
ARA II	3.6 (1.77-7.52)	0.004*		
Age > 60 years	4.6 (2.22-9.68)	< 0.001 *	3.9(1.42-6.71)	0.004
Troponin I > 0.205 ng/mL	1.6 (0.83-3.37)	Ns		
SVO2 %	0.6 (0.3-1.3)	Ns		
Prone position days	0.3 (0.08-1.5)	Ns		
Lactate > 2.5 mmol	2.8 (1.11-7.23)	0.02*		
VO2 < 250ml	1.0 (0.49-2.15)	Ns		
BNP> 150 pg/mL	2.4 (1.16-5.25)	0.01*		
PaO2/FIO2 <100	3.4 (1.37-8.76)	Ns		

\*Variables with statistical significance p< 0.05. Logistic regression models, COPD: Chronic Obstructive Pulmonary Disease; SVO2: Central venous oxygen saturation; VO2: Oxygen Consumption; BNP: Brain Natriuretic Peptide; ARA II: Angiotensin II receptor blockers.

**Table 4:** Characteristics associated with mortality in patients with Sars-CoV-2 virus infection.



**Figure 1:** Forest plot risk of death in patients with cardiovascular complications associated with SARS-COV-2 virus infection in Intensive Care.

## Discussion

While the perspective of SARS COV-2 pneumonia has focused on pulmonary complications, it is important for clinicians to be aware of cardiovascular complications, which can be a significant contributor to the mortality associated with this disease [12]. Jiang Y and collaborators in a retrospective observational study with a total of 281 patients all older adults diagnosed with COVID-19. They mention that in an age range of 60-79 years there is a mortality rate of 33.5%, which increases proportionally as age increases. Regarding the results in this study agrees with the reported age, which is in over 60 years (OR 3.9, 95% CI, 1.42-6.71, p 0.004). Likewise, in the results of Jiang Y, and collaborator in his binary logistic regression analysis, they showed that cardiovascular comorbidities such as systemic arterial hypertension, diabetes and COPD, were independent risk factors that were significantly associated with mortality, the same risk factors identified in the present study [13]. Paloma Ferrando-Vivas and collaborators in their observational cohort study with a sample of 10,362 patients diagnosed with COVID-19. They mention that the probability of dying within 30 days increased with values less than 50 mmHg PaO<sub>2</sub>/FiO<sub>2</sub> in patients on mechanical ventilation (HR 1.21), together with hyperlactatemia more than 2 mmol / L with (HR 1.49) with a p< 0.0001. Similarly, in this study it was detected that a lactate greater than 2.5 mmol/L (OR 2.8, 95% CI 1.11-7.23, p 0.02) showed a significant association as a predictor of mortality [14]. Randy J. Ip, and collaborators conducted a cohort with a mortality rate of 46.2%, where variables were adjusted by multiple logistic regression finding that atrial fibrillation contributed to higher mortality with a (OR 4.8, p 0.004) In our study the outcome of atrial fibrillation was associated with the consumption of ARA2 (OR 4.9, 95% CI 1.03-23.9, p<0.05), presenting as a relevant factor for mortality in patients [15]. Kevin K. Manocha et al. conducted an observational cohort study of 1053 COVID-19 patients. Patients had the following biomarkers measured: troponin I, B-type natriuretic peptide, C-reactive protein, ferritin, and d-dimer (n 446). The primary endpoint was 30-day in-hospital mortality. Troponin I ≥0.34 ng/ml was the only independent predictor of 30-day mortality (adjusted OR, 4.38; P<0.001). Patients were also stratified based on the hypoxia, age and troponin score (HA2T2), patients with a score ≥ 3 had a mortality at 30 days of 43.7%, while those with a score < 3 had a mortality of 5.9%. These results are comparatively significant since the results of this study documented the presence of elevated levels of troponin I 0.205 ng/dl (OR 4.3, 95% CI 1.31-14.17, p 0.014) associated with the cardiovascular outcome of heart failure type, was associated with the elevation of Pro-BNP above 150 pg./ml (OR 4.9, CI95% 1.60 - 15.28, p 0.004). In turn, mortality was adjusted with cardiovascular outcomes, showing Heart Failure (OR 15.81, 95% CI 2.00-124.91, p 0.009) as a factor associated with mortality. Therefore, elevated troponin concentrations are a potent predictor of in-hospital

mortality in patients with cardiovascular complications [16]. Kim Min Seo, and collaborators in their study of a systematic review and meta-analysis on the use of hydroxychloroquine, demonstrated that the combination of hydroxychloroquine and azithromycin is associated with a higher incidence of QT prolongation (OR 2.01; 95% CI 1.26 to 3.20; p 0.003) In our study as a result no mortality association was observed with the isolated treatment of Hydroxychloroquine (OR 1.02, 95% CI 0.50-2.07, p 0.93), Hydroxychloroquine plus Azithromycin (OR 1.00, 95% CI 0.48-2.05, p 1.00), and Hydroxychloroquine plus Ivermectin (OR 0.75, 95% CI 0.33-1.69, p 0.48), however, regarding cardiovascular outcome, heart failure was associated with treatment with hydroxychloroquine (OR 3.2, CI95% 1.08 – 9.49, p <0.05) [17]. Finally, we point out that the present study design is only useful to see prevalence's and statistical associations that suggest a possible risk, and not to determine pharmacological treatment schemes or therapeutic measures.

## Conclusion

Mortality was associated with males over 60 years of age with a history of Diabetes Mellitus, Systemic Arterial Hypertension, Chronic Obstructive Pulmonary Disease, smoking, prior treatment with ARA2, lactate greater than 2.5 mmol/L, Pro-BNP greater than 150 pg/ml, and PaO<sub>2</sub>/FiO<sub>2</sub> index less than 100. Cardiac failure outcome was associated with elevation of Troponin I above 0.205 ng/dl, Pro-BNP above 150 pg/ml, and treatment with hydroxychloroquine. No association with mortality was observed with treatment based on Hydroxychloroquine, Hydroxychloroquine plus Azithromycin, and Hydroxychloroquine plus Azithromycin plus Ivermectin, highlighting that more than 90% of the population received treatment with steroids and anticoagulants.

## References

1. Ge H, Wang X, Yuan X, Xiao G, Wang C, et al (2020) The epidemiology and clinical information about COVID-19. *Eur J Clin Microbiol Infect Dis.* 39: 1011-1019.
2. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19) Corporate Authors(s): National Center for Immunization and Respiratory Diseases (U.S.), Division of Viral Diseases, Published Date: June 30, 2020 Series: Coronavirus Disease 2019 (CoVID-19).
3. Miller R, Englund K (2020) Transmission and risk factors of COVID-19. *Cleve Clin J Med.*
4. Tikellis C, Thomas MC (2012) Angiotensin-Converting Enzyme 2 (ACE2) Is a Key Modulator of the Renin Angiotensin System in Health and Disease. *Int J Pept.* 2012: 256294.
5. Zheng YY, Ma YT, Zhang JY, Xie X (2020) COVID-19 and the cardiovascular system. *Nat Rev Cardiol.* 17: 259-260.
6. Akhmerov A, Marbán E (2020) COVID-19 and the Heart. *Circ Res.* 126: 1443-1455.

7. Bansal M (2020) cardiovascular disease and COVID-19. *Diabetes Metab Syndr.* 14: 247-250.
8. Buzon J, Roignot O, Lemoine S, Perez P, Kimmoun A, et al (2015) Takotsubo Cardiomyopathy Triggered by Influenza A Virus. *Intern Med.* 54: 2017-2019.
9. Murthy S, Gomersall CD, Fowler RA (2020) Care for Critically Ill Patients with COVID-19. *JAMA.* 323: 1499-1500.
10. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, et al (2020) Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. *J Am Coll Cardiol.* 75: 2352-2371.
11. Danzi GB, Loffi M, Galeazzi G, Gherbesi E (2020) Acute pulmonary embolism and COVID-19 pneumonia: a random association? *Eur Heart J.* 41: 1858.
12. Long B, Brady WJ, Koyfman A, Gottlieb M (2020) cardiovascular complications in COVID-19. *Am J Emerg Med.* 38: 1504-1507.
13. Jiang Y, Abudurexiti S, An MM, Cao D, Wei J, et al (2020) Risk factors associated with 28-day all-cause mortality in older severe COVID-19 patients in Wuhan, China: a retrospective observational study. *Sci Rep* 10: 22369.
14. Ferrando-Vivas P, Doidge J, Thomas K, Gould DW, Mouncey P, et al (2021) ICNARC COVID-19 Team, Prognostic Factors for 30-Day Mortality in Critically Ill Patients With Coronavirus Disease 2019: An Observational Cohort Study. *Crit Care Med.* 49: 102-111.
15. Randy Jlp, Ali A, Baloch ZQ, Al-Abcha A, Jacob C, et al (2021) Atrial Fibrillation as a Predictor of Mortality in High Risk COVID-19 Patients: A Multicentre Study of 171 Patients. *Heart Lung Circ.* 30: 1151-1156.
16. Manocha KK, Kirzner J, Ying X, Yeo I, Peltzer B, et al (2021) Troponin and Other Biomarker Levels and Outcomes Among Patients Hospitalized With COVID-19: Derivation and Validation of the HA2T2 COVID-19 Mortality Risk Score. *J Am Heart Assoc.* 10: e018477
17. Kim MS, An MH, Kim WJ, Hwang TH (2020) Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: A systematic review and network meta-analysis. *PLoS Med.* 17: e1003501.