How to Cite:
Kamal, H. M., El-Araby, M. E.-S., Salem, A. S., & Sanad, A. M. (2023). Relation between clinical status and right ventricular changes in corona virus disease 19 patients. *International Journal of Health Sciences*, *7*(S1), 3246–3255. Retrieved from https://sciencescholar.us/journal/index.php/ijhs/article/view/14849

Relation between clinical status and right ventricular changes in corona virus disease 19 patients

Hanan M. Kamal
Professor of Cardiovascular medicine /Faculty of Medicine – Suez Canal University

Mohamed El-Sayed El-Araby
Cardiovascular Resident, Al-Mokattam Hospital for Health Insurance

Ahmed Salah Salem
Assistant Professor of Cardiovascular medicine /Faculty of Medicine – Suez Canal University

Ahmed Mohamed Sanad
Lecturer of Cardiovascular medicine/Faculty of Medicine – Suez Canal University

***Abstract*---**Background: Role of laboratory parameters in prediction of COVID-19 severity and correlations with cardiac assessment is not well established and needs further investigations. This study was carried out to assess relation between clinical status and right ventricular changes in corona virus disease 19 patients using 2D echocardiography. Patients and methods: This cross sectional study was conducted on one hundred hospitalized COVID-19 PCR-positive patients with mild, moderate, or severe symptoms who were admitted to AL-MOKATTAM Health Insurance Hospital. Patients were subjected to detailed history taking, clinical examinations, laboratory investigations and transthoracic echocardiography. Results: In this study 100 Covid 19 patients (72 males and 28 females) with mean age of 63.13 ± 9.4 years (range: 33 – 86 years). The lab values are within normal ranges except oxygen saturation which was lower than normal values. The significant risk factors included hypertension, DM, smoking and dyslipidemia, the most prominent was dyslipidemia (50%), followed by smoking (33%), then hypertension (21%) and diabetes mellitus (15%). Relation of RV abnormality was associated with lymphocytes count, CKMB (creatinine kinase myocardial band), CRP, D-Dimer and ferritin (P: 0.005, P:0.001, P:0.000, P:0.017, P:0.015, respectively). Also, RV abnormality was associated with positive troponin (P<0.000). Conclusion: In our COVID-19 patients,

the severity of COVID-19 symptoms, the CT severity score, DM, CRP, D-dimer, and LVESD were all predictors to RV dysfunction.

***Keywords*---**COVID-19, RV dysfunction, CRP, D-dimer.

Introduction

A new strain of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified in March 2020, and the illness quickly spread around the world [1]. Acute respiratory distress syndrome (ARDS) is the primary outcome of COVID-19, a new virus that can range in severity from asymptomatic to life-threatening illness with a predominance of lung involvement. However, reports of cardiovascular involvement have surfaced, both during infection and after resolution, as details of COVID-19 become clearer [2]. Furthermore, research have indicated that regardless of the severity of the illness, most individuals who have COVID-19 infections experience cardiac consequences of some form [3].

It has been hypothesized that the angiotensin converting enzyme (ACE) II receptor serves as the entry point for the SARS-CoV-2 virus into the body. The pulmonary alveoli are the primary site of ACE receptor expression, and the heart is the second organ with the greatest concentration of ACE receptors. Notably, cardiac involvement during COVID-19 infection is associated with poorer results and increases mortality [4].

Ventricular dysfunction, coronary artery dilatation or aneurysms, and seldom pericarditis and valvulitis, constitute the cardiac involvement in the majority of studies in patients with COVID 19 [5]. An inexpensive and frequently available technique for evaluating the structure and operation of the heart is echocardiography. In critically ill patients, a targeted examination can provide important information that may affect therapy choices [6]. Thus, this study was conducted to assess relation between clinical status and right ventricular changes in corona virus disease 19 patients using 2D echocardiography.

Patients and Methods

The study was conducted on one hundred hospitalized COVID-19 PCR-positive patients with mild, moderate, or severe symptoms who were admitted to AL-MOKATTAM Health Insurance Hospital between April 2021 and April 2022. A total of eight patients were excluded from the study due to their poor echogenic windows, refusals to participate in the study, history of cardiovascular disease, or mild, moderate, or severe COVID-19 infection.

Patient was admitted to the hospital after a 72-hour PCR test revealed a positive COVID-19 infection, male or non-pregnant female adult who was at least 18 years old when they enrolled, and patients with any length of symptoms indicative with COVID-19, including at least one of the following (imaging-based radiographic infiltrations (chest x-rays, CT scans, etc.); OR SpO2 <= 94% in room air or needing extra oxygen) were included in the study. Patients with past history of acute myocardial infarction or acute arrhythmia or a 72-hour notice of expected

hospital release or transfer to a different hospital that is not a study site or patients with pulmonary embolism were excluded from the study.

A positive reverse-transcriptase polymerase chain reaction test for COVID19 respiratory syndrome coronavirus in a respiratory tract sample verified the diagnosis of COVID-19 infection in all patients. The Chinese National Health Commission released recommendations for the diagnosis and treatment of COVID-19 on February 18, 2020, and they were followed for the patients with mild, moderate, and severe cases who were recruited in this study [5].

Patients were subjected to detailed history taking, clinical examinations and Laboratory findings were systematically recorded (including CBC, INR, renal function, liver function, troponin I, CK, CKMB, D dimer, CRP, ferritin and ABG. The patients were assessed (0-25) by two expert radiologists according to the level of lobar involvement in chest CT as shown in table 1. These gradings were utilized to construct 3 COVID-19severity groups. A thorough transthoracic echocardiography performed by cardiologists skilled in the recording and interpretation of echocardiograms using the same device (GE Vivid S6).

Typical transthoracic echocardiogram in two dimensions: Using, the echocardiographic investigation was conducted. Ultrasonic apparatus: This investigation employed a GE vivid S6 with a 3S-RS Phased Array Transducer operating at 3.5 GHz. The following techniques were used to evaluate the right ventricle:

I. RV measurements: RV dimensions were calculated using an apical four-chamber image with a focus on the RV.RV dilatation is often indicated by a diameter more than 41 mm at the base and greater than 35 mm at the mid-level in the RV-focused image. Maximum transversal dimension = basal RV linear dimension (RVD1) The level of the papillary mussels at the end diastole in the basal one-third of the RV flow is equal to the transverse RV diameter in the middle third of the RV flow, or almost midway between the maximal basal diameter and the apex.
II. Right ventricular systolic function: The following methods were used to assess RV systolic function [7].
    1. TAPSE (trans annular plane systolic excursion): It was measured by M-mode echocardiography with the cursor optimally align along the direction of the tricuspid lateral annulus in the apical four-chamber view (normal value>17 mm),
    2. RV 2D FAC (fractional area change):from RV-focused apical four chamber view, RV FAC(%)=100× (EDA-ESA)/EDA. While tracing the RV area, care must be taken to include the trabeculae in the RV cavity (normal value>35%).
    3. RV MPI(Right Ventricular Myocardial performance index): Pulsed wave TDI was placed at the lateral tricuspid annulus to measure the peak velocities of IVC (IVC max), S wave (S max), E′, A′ waves and E′/A′ ratio also the duration of IVC, IVR, time to peak of IVC, S wave duration were measured. RV MPI: MPI=(IVCT+IVRT/)ET.

4. Lateral annular velocity (RV S'): using right ventricular dimension using right ventricle basal diameter measured in the apical 4-chamber view (10).RV systolic dysfunction is defined as S′ velocity < 9.5 cm/sec by TDI.

In compliance with the most recent recommendations [8]. To lessen the chance of infection, the following steps were taken: Every echocardiography test was performed at the bedside of a COVID-19 patient who was admitted to the hospital with authorization. These echocardiography scanners were set aside for the COVID-19 critical care unit to lessen the risk of infection transmission. During the echocardiographic recordings, personal protective equipment (PPE) was utilized, including N-95 respirator masks, fluid-resistant gowns, two pairs of gloves, head coverings, eye shields, and shoe covers. All measurements were made offline and there was no ECG monitoring utilized during imaging in order to reduce exposure and contamination.

Statistical analysis

The statistical software for the social sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA) was used to code and input the data. For quantitative data, the mean, standard deviation, median, and interquartile range were used; for categorical data, the frequency (count) and relative frequency (%) were used. The non-parametric Mann-Whitney test was used to compare numerical variables. We used the Chi square (2) test to compare categorical data. When the anticipated frequency is less than 5, an exact test was employed instead, and P-values less than 0.05 were regarded as statistically significant.

Ethical approval

Every case-sharing participant in the study provided his or her consent. Any patient who was mulling over taking part in this research was given a thorough explanation of all the steps, presented in a manner they could fully comprehend. The Ethical Committee Council of Suez Canal University approved the study. The study was done in compliance with the Declaration of Helsinki, which is the World Medical Association's code of ethics for studies for humans.

Results

This study included 100 COVID 19 patients with mean ±SD age of 63.13 ± 9.4 years and 72 males (72%) and 28 females (28%). The participants' ages ranged from 33 to 86 years. In figure 1, there was significant risk factors that include hypertension, diabetes mellitus, smoking and dyslipidemia, the most prominent was dyslipidemia (50%), followed by smoking (33%), then hypertension (21%) and diabetes mellitus (15%).

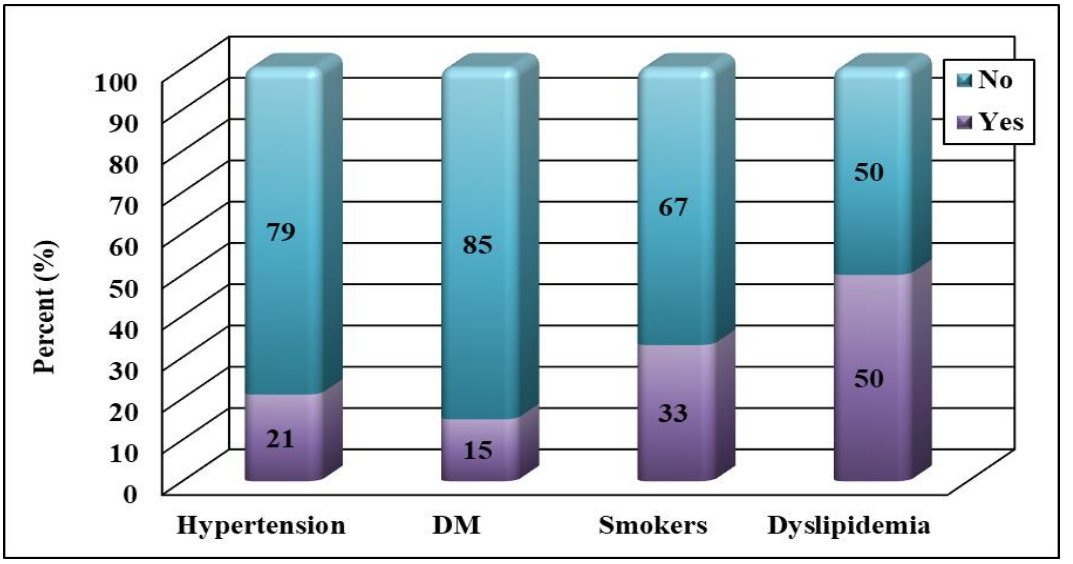

Figure 1: Risk factors of the studied population

In figure 2, 8 patients (8%) mild respiratory involvement,76 patients (76%) had moderate respiratory involvement and 16 patients (16%) had severe respiratory involvement.

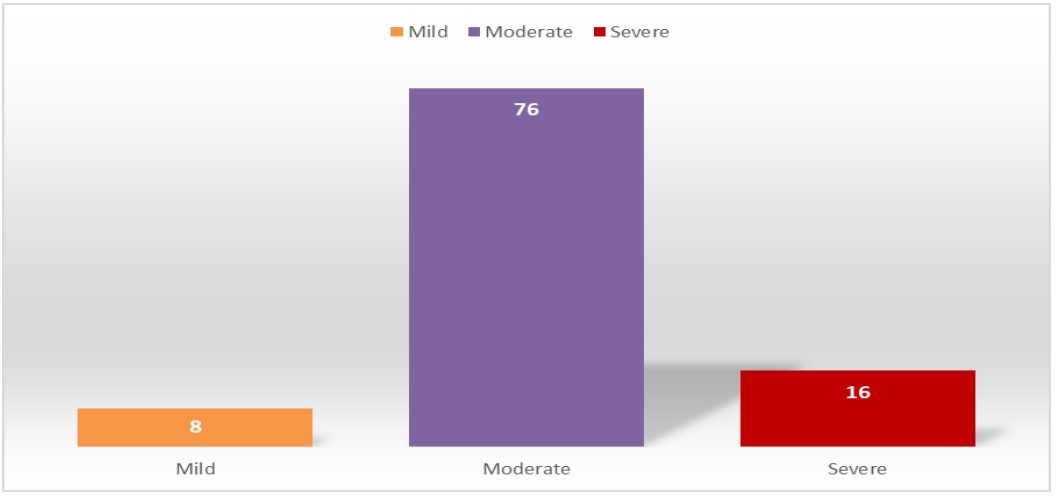

Figure 2: Severity grading distribution among the study patients.

In table 1, the clinical characteristics of the studied populations. All mean values are within normal ranges except oxygen saturation which was lower than normal values.

Table 1: Clinical characteristics of the studied population

	Range		Mean ±SD	
	Min	Max	Mean	SD
SBP (mmHg)	102	176	134.87	9.608
DBP (mmHg)	58	88	75.48	7.263
Pulse (beat/min)	80	120	98.85	8.835
BMI (kg/m^2)	21	37	27.33	3.412
BSA (m^2)	1.2	2.6	1.818	0.275
O_2 saturation	51	95	79.57	9.580

SBP: systolic blood pressure, DBP: diastolic blood pressure, BMI: body mass index, BSA: body surface area, SD: standard deviation.

Figure 3 illustrated the complications of our patients such as number of patients on mechanical ventilation (13%), number of patients who has tachyarrhythmia (10%) whether atrial or ventricular, deep venous thrombosis (2%) and who had shock (2%).

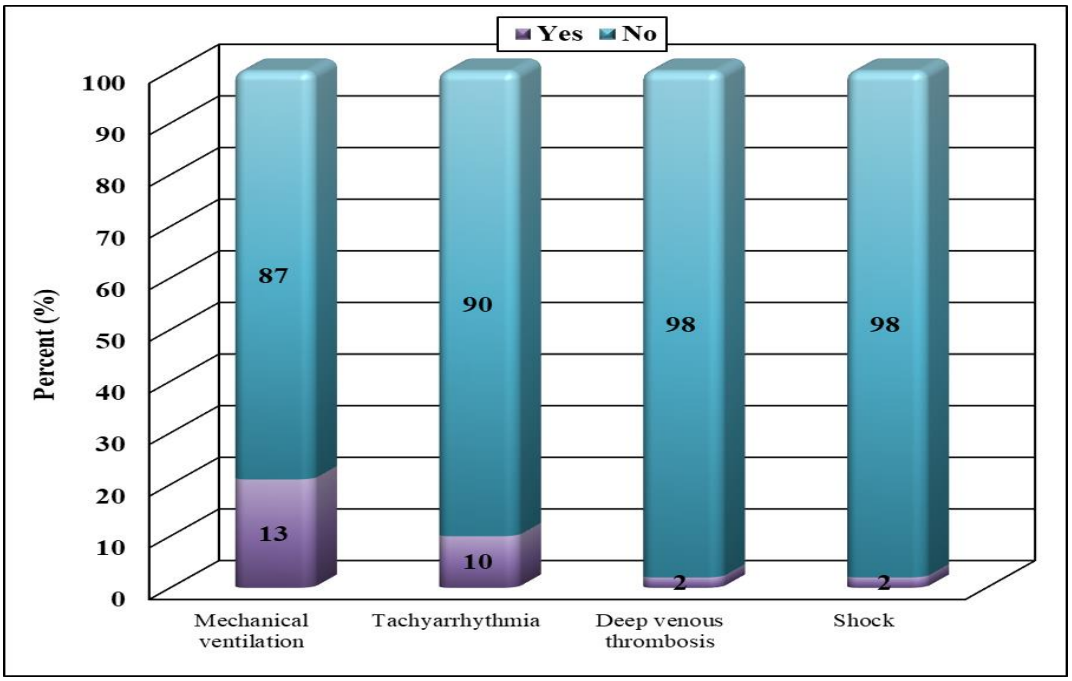

Figure 3: Complications of the studied population.

In table 2, RV abnormality was associated with lymphocytes count, CKMB (creatinine kinase myocardial band), CRP, D-Dimer and ferritin (P: 0.005, P:0.001, P:0.000, P:0.017, P:0.015, respectively). Also, RV abnormality was associated with positive troponin (P<0.000).

Table 2: Relation of RV abnormality (RV dilatation and systolic dysfunction) and laboratory findings

Finding	RV dilatation		Systolic dysfunction	
	r	P	r	P
FBG (g/dL)	0.1467	0.058	0.1319	0.061
PPBG (g/dL)	0.1421	0.052	0.1463	0.059
HbA1c	0.1456	0.055	0.1421	0.052
Total cholesterol (mg/dl)	0.1315	0.062	0.1205	0.066
HDL (mg/dl)	-0.0912	0.081	-0.0961	0.078
LDL (mg/dl)	0.1195	0.067	0.1218	0.064
Triglycerides (mg/dl)	0.0846	0.092	0.0887	0.089
Serum creatinine	0.0127	0.317	0.0142	0.272
Creatinine clearance	0.0185	0.147	0.0189	0.126
SGOT (U/L)	0.0136	0.294	0.0397	0.312
SGPT (U/L)	0.0121	0.324	0.0112	0.337
Total leucocytic count	0.0163	0.132	0.0197	0.124
Lymphocytes count	0.4251	0.005*	0.3897	0.006*
Hemoglobin concentration	0.0207	0.111	0.0163	0.132
Platelets	0.0142	0.214	0.0399	0.311
INR	0.1422	0.052	0.1453	0.056
CK	0.1461	0.054	0.1425	0.051
CKMB	0.5134	0.001*	0.5194	0.001*
Urea	0.0133	0.423	0.0072	0.374
Phosphorus	0.0024	0.758	0.0021	0.762
PCO_2	0.1319	0.061	0.1465	0.059
PO_2	-0.1456	0.055	-0.1458	0.054
HCO_3	0.1312	0.063	0.1309	0.065
C-reactive protein	0.6751	0.000*	0.5928	0.000*
D-Dimer	0.2716	0.017*	0.2652	0.021*
Serum Ferritin	0.2811	0.015*	0.2797	0.018*
Positive troponin	0.7134	0.000*	0.9623	0.000*

In table 3, predictors of right ventricular dysfunction in COVID19 patients are, elevation of CT severity score, severity of Covid-19 manifestation, DM, CRP, D-dimer and LVESD in Covid-19 patients

Table 3: Logistic regression analysis for predictors of right ventricular dysfunction in COVID19 patients

Variables	B	SE	Wald	OR	95%-CI	P
Age (years)	0.19	0.0298	0.173	1.21	1.14, 1.28	0.994
Sex	0.21	0.0541	0.165	0.86	0.44, 1.71	0.674
CT severity	0.13	0.0473	0.167	1.06	1.01, 1.10	0.009*
Disease Severity	0.60	0.0559	0.164	1.06	1.00, 1.11	0.040*
DM	0.57	0.0542	0.165	1.76	1.58, 1.96	0.003*
CRP	0.17	0.0497	0.166	1.19	1.08, 1.31	0.035*
D-dimer	0.11	0.0842	0.136	1.12	0.95, 1.32	0.048*
Lymphocyte count	0.17	0.0530	0.343	0.91	0.81, 1.03	0.123

LVESD	0.16	0.0532	0.346	2.2	1.14, 4.39	0.020*
LVEDD	0.16	0.0734	0.179	1.64	1.02, 2.65	0.095
LA Diameter	0.49	0.2445	0.256	1.33	1.15, 1.53	0.108
LVEF	0.25	0.0728	0.139	1.29	1.19, 1.48	0.050

Discussion

As long as the pandemic persists, further research is needed to properly understand the cardiovascular implications of COVID-19, a complicated and dynamic multi-organ illness. Longer-term follow-up data will be necessary to completely comprehend the real cardiovascular consequences of this, especially in relation to the prevalence of heart failure and the burden of coronary ischemia [9]. In light of the current pandemic, efforts are concentrated on recognizing acute cardiac problems, which are more prevalent in individuals with advanced illness and are linked to a higher death rate [10]. According to reports, COVID-19 has so far caused myocarditis, heart failure, pulmonary embolism (PE), arrhythmia, sudden death, pulmonary hypertension, and ST elevation myocardial infarction [11].

So this study was conducted to assess relation between clinical status and right ventricular function parameters using 2D echocardiography. The study included 100 Covid-19 patients, with a mean age of 63.13 ± 9.404 years (range: 33 – 86 years) and 72 men (72%) and 28 females (28%). With the exception of oxygen saturation, which was below average, all test results are within normal levels. DM, smoking, dyslipidemia, and hypertension were the main risk factors. Dyslipidemia was the most common risk factor, accounting for 50% of the total, followed by smoking (33%), hypertension (21%), and diabetes mellitus (15%). The mean duration of MV for thirteen percent (13%) of the patients was 2.286 days. Patients had shock (2%), DVT (2%), and tachyarrhythmia (10%). A mean of 13.86 for the Chest CT severity score was also shown.

A comparable research was conducted by Bleakley et al. [9] on ninety-nine Covid-19 patients at the Royal Brompton Hospital in London, UK. The cohort's mean age was 52.0 ± 10.8 years, with 25.6% of the sample being female. The most common comorbidities were diabetes mellitus and hypertension, with 22.2% and 36.7% of the sample having each condition, respectively, and 22.3% of the sample being treated with an angiotensin receptor blocker or an angiotensin converting enzyme inhibitor.

RV abnormality (RV systolic dysfunction in the form of FAC) and lab results were significantly correlated ($p > 0.05$). The following lab results were statistically significant ($p < 0.05$): lymphocyte count, CKMB (creatinine kinase myocardial band), CRP, D-Dimer, S. Ferritin, and positive troponin (P: 0.005, P:0.003, P:0.001, P:0.017, P:0.015, and P:0.001, respectively. Similar findings were reported by Mahmoud-Elsayed HM et al. [12] who found that patients with positive troponin, CRP, D-Dimer, and lymphocyte count had substantial RV systolic dysfunction (FAC).

Kiss et al. [13], who found a statistically significant correlation between RV dilation/systolic dysfunction and death in a sample of 115 patients, provided

more evidence of RV involvement in COVID-19. Elevated Troponin levels were indicative of myocardial damage in patients with RV dysfunction. The current investigation found that elevated CT severity score, the severity of Covid-19 manifestation, DM, CRP, D-dimer, and LVESD in Covid-19 patients were significant predictors of right ventricular dysfunction (RV dysfunction).

Although the correlation was not as strong statistically, TAPSE was associated with lower RV FAC. In a subgroup the study shows an association between RV free wall strain and RV (FAC) and RV end-systolic area index (RVESAI). This suggests that RV free wall strain may serve as a predictor of RV dysfunction in COVID-19 patients. However, this is only one study, and more research is needed to confirm this finding and to determine the role of RV free wall strain as a predictor of RV dysfunction in COVID-19 patients. It is important to consider all factors, including underlying medical conditions such as diabetes mellitus, when assessing the risk of RV dysfunction in COVID-19 patients. RV FAC/RVSP was also linked to PEEP, ALT, and the partial pressure of inspired oxygen to oxygen (PaO_2/FiO_2) ratio. D-dimer, CRP, and hs-TnI did not connect with it [9].

RV abnormalities were identified in 185 of the 1216 Covid-19 patients examined by Bleakley et al. [9]. In contrast to these findings, there was no correlation found between the occurrence of RV dysfunction and biomarker increase (troponin or natriuretic peptides). The study did not identify the precise patterns of RV impairment or the criteria that were employed to assess RV function. On the other hand, prior findings from single center investigations with Covid-19 populations that are not essential consistently reveal a loss in RV longitudinal function as opposed to radial function.

Despite the study's findings, there are certain restrictions. First of all, each patient in this experiment had Covid-19 validated. It is not possible to directly compare our findings with patient groups with RV difficulties in other research since no control data from non-Covid trials were available. Second, although though the sample size is larger than many previous studies, it is still very small and vulnerable to the inherent limitations of smaller cohorts. Thirdly, it is recommended that future studies confirm the connections we have found in cohorts similar to our own.

Conclusion

In our COVID-19 patients, the severity of COVID-19 symptoms, the CT severity score, DM, CRP, D-dimer, and LVESD were all predictive with RV dysfunction.

References

1. Võ PMT, Đinh CT, Nguyễn NTL, Lý ĐH, Trang VP, Phạm TKĐ, Hoàng TBN. 1. Coronavirus disease (COVID-19) – World Health Organization. Accessed March 3, 2023. https://www.who.int/emergencies/diseases/novel-coronavirus-2019 2. Mathieu E, Ritchie H, Rodés-Guirao L, et al. Coronavirus Pandemic (COVID-19). Our World in Data. Publ. Tạp chí Y học Việt Nam [Internet]. 2023;527(2).
2. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al.

Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. JAMA [Internet]. 2020 Jul 21;324(3):259–69.
3. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute Heart Failure in Multisystem Inflammatory Syndrome in Children in the Context of Global SARS-CoV-2 Pandemic. Circulation [Internet]. 2020;142(5):429–36.
4. Leeb RT, Price S, Sliwa S, Kimball A, Szucs L, Caruso E, et al. COVID-19 Trends Among School-Aged Children - United States, March 1-September 19, 2020. MMWR Morb Mortal Wkly Rep [Internet]. 2020 Oct 2;69(39):1410–5.
5. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: a review. JAMA Cardiol. 2020;5(7):831–40.
6. Keller M, Magunia H, Rosenberger P, Koeppen M. Echocardiography as a Tool to Assess Cardiac Function in Critical Care-A Review. Diagnostics (Basel, Switzerland). 2023 Feb;13(5).
7. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr [Internet]. 2015;28(1):1-39.e14.
8. Kirkpatrick J, 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. J Indian Acad Echocardiogr & Cardiovasc Imaging [Internet]. 2020;4(1):137–43.
9. Bleakley C, Singh S, Garfield B, Morosin M, Surkova E, Mandalia MS, et al. Right ventricular dysfunction in critically ill COVID-19 ARDS. Int J Cardiol. 2021;327:251–8.
10. Peng F, Tu L, Yang Y, Hu P, Wang R, Hu Q, et al. Management and Treatment of COVID-19: The Chinese Experience. Can J Cardiol [Internet]. 2020/04/17. 2020 Jun;36(6):915–30.
11. Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, Shah B, et al. ST-Segment Elevation in Patients with Covid-19 - A Case Series. N Engl J Med [Internet]. 2020/04/17. 2020 Jun 18;382(25):2478–80.
12. Mahmoud-Elsayed HM, Moody WE, Bradlow WM, Khan-Kheil AM, Senior J, Hudsmith LE, Steeds RP. Echocardiographic Findings in Patients With COVID-19 Pneumonia. Can J Cardiol [Internet]. 2020/05/28. 2020 Aug;36(8):1203–7.
13. Kiss S, Gede N, Hegyi P, Németh D, Földi M, Dembrovszky F, et al. Early changes in laboratory parameters are predictors of mortality and ICU admission in patients with COVID-19: a systematic review and meta-analysis. Med Microbiol Immunol. 2021 Feb;210(1):33–47.