



Can Cardiac Indices in Computed Tomography (CT) Scan Predict COVID-19 Clinical Outcome?

Somayeh Livani ¹, Mojtaba Samimi ^{1,*}, Farnaz Hooshmand ¹ and Mohammad Mohajer Tabrizi ²

¹Clinical Research Development Center (CRDC), Sayad-Shirazi Hospital, Golestan University of Medical Sciences, Gorgan, Iran

²Faculty of Engineering, Golestan University, Gorgan, Iran

*Corresponding author: Clinical Research Development Center (CRDC), Sayad-Shirazi Hospital, Golestan University of Medical Sciences, Gorgan, Iran. Email: mojtaba.samimi70@gmail.com

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Abstract

Background: Assessing the measurable chest computed tomography (CT) scan cardiac parameters can help us evaluate cardiovascular involvement and risk stratification in patients with coronavirus disease 2019 (COVID-19).

Objectives: This study investigated the measurable chest cardiac CT indices and their association with predicting outcomes in patients with COVID-19.

Patients and Methods: Patients with confirmed COVID-19 were included in the study from March up to June 2020 and underwent chest CT scans on admission. The following parameters were analyzed: The extent and pattern of lung involvement, cardiothoracic ratio (CTR), pulmonary artery to aorta ratio (PA/A), pericardial effusion, pleural effusion, and inferior vena cava (IVC) diameter through low-dose CT scan. The association between cardiac indices and patients and the extent of lung involvement outcome was evaluated by logistic regression, Cox regression, and linear regression, respectively.

Results: A total of 176 COVID-19 patients (51.1% men and 48.9% women) were enrolled in the study. Of them, 55 patients (31.25%) died, and 121 patients were discharged (68.75%). The mean age of participants was 64.9 ± 15.09 years. $CTR > 0.49$ was more frequent among deceased patients (50.9% vs. 31.4%, $P = 0.018$) and was associated with non-significant increases in odds ratio (OR) and hazard ratio (HR) ($OR = 1.75$, $P = 0.11$; $HR = 1.43$, $P = 0.19$). Moreover, $PA/A > 1$ was more common in deaths (52.7% vs. 32.2%; $P = 0.012$) and significantly increased OR but not HR ($OR = 1.99$; $P = 0.04$; $HR = 1.36$; $P = 0.26$). The moderate and severe pleural effusion was noticeably associated with prolonged hospitalization ($HR = 4.09$, $P = 0.01$; $HR = 3.37$, $P = 0.02$, respectively). The IVC diameter and pericardial effusion were not significantly correlated with outcomes.

Conclusion: Cardiac indices in chest CT of COVID-19 patients can be accounted for the prediction of patient outcomes in the clinic, such as $PA/A > 1$ ratio, which increases the likelihood of in-hospital deaths.

Keywords: COVID-19, Computed Tomography, Cardiac Computed Tomography, Cardiothoracic Ratio, Pulmonary Artery to Aorta Ratio, Cardiac Indices, Cardiovascular Diseases

1. Background

The coronavirus disease 2019 (COVID-19) is a complex viral condition that predominantly involves multiple organs, such as the respiratory and cardiovascular systems (1, 2). Although the majority of the patients experience a moderate form of the disease, small groups develop acute respiratory distress syndrome (ARDS) and multi-organ dysfunctions (3). According to recent studies, patients with underlying cardiovascular diseases (CVD) are more likely to develop complications and experience a more severe clinical course of the disease. Furthermore, numerous reports of cardiovascular complications among patients

without a CVD history may contribute to poor disease outcomes (4, 5).

The main known mechanism for COVID-19 cardiovascular toxicity is the expression of angiotensin-converting enzyme-2 (ACE-2) in cardiomyocytes. When SARS-CoV-2 binds to its cellular target, ACE2 receptors, myocardial infection occurs. SARS-CoV-2 also may induce endothelial cell apoptosis, leading to microvascular dysfunction that is a predisposing factor for developing thromboembolic events. The following hypoxemic mechanisms will lead to further damage (6). Well-known COVID-19 cardiac manifestations can be named myocardial infarction,

myocarditis, arrhythmias, cardiomyopathy, pulmonary embolism, and deep vein thrombosis (7-9).

The modality of choice for COVID-19 diagnosis is the real-time reverse transcription polymerase chain reaction (RT-PCR) test (10). Moreover, chest computed tomography (CCT) is an imaging method with high sensitivity that has been widely used in healthcare centers to stratify the severity of the disease and evaluate pulmonary and extrapulmonary complications (11). It has been demonstrated that some imaging-based parameters comprising cardiac indices can predict the severity of the disease and the risk of morbidity and mortality in different stages of the disease (10). An elevated cardiothoracic ratio (CTR) that indicates cardiomegaly (12), an increased pulmonary artery to the aorta (PA/A) ratio that can be a sign of pulmonary hypertension, inferior vena cava (IVC) dimension, and pericardial effusion all were compatible with poor prognosis in patients with COVID-19 (10, 13). These indices may also indicate an increased risk of CVD secondary to COVID-19 (14, 15).

2. Objectives

Investigating the CT-based pulmonary and extrapulmonary prognostic parameters, along with the clinical course of the disease, can help us to determine disease severity and stratify the risk of mortality and morbidity among COVID-19 patients and can play an important role in patient management, especially for early interventions. Therefore, this study aimed to investigate CT-based cardiac indices as prognostic factors in predicting outcomes among hospitalized patients with COVID-19.

3. Patients and Methods

3.1. Study Design

This descriptive-analytical study was conducted in Gorgan, northern Iran, from March 2020 up to June 2020. Participants included patients with a confirmed diagnosis of COVID-19 who were admitted to Shahid Sayad Shirazi Hospital. All the patients in the study were managed according to diagnostic and management guidelines of Iran's Ministry of Health and Medical Education (MoHME) that were released during the study period. The summary of management strategies was as follows. Patients with mild COVID-19 received supportive care and were managed in the outpatient setting. Patients with moderate to severe disease were admitted to the hospital and then received supportive care, oxygen therapy, corticosteroids (dexamethasone), anticoagulants

(heparin and enoxaparin), and remdesivir if they had moderate to severe lung involvement. Then, patients were monitored for further therapeutic options such as intubation and intensive care unit admission.

The present study was approved by the Ethics Committee of Golestan University of Medical Sciences (ID: IR.GOUMS.REC.1400.214). Informed consent was obtained from all individuals who were enrolled in the study. All investigations were in accordance with the Declaration of Helsinki Declaration.

3.2. Inclusion and Exclusion Criteria

Inclusion criteria included (1) patients with confirmed COVID-19 diagnosis through positive RT-PCR test; and (2) age older than 18 years. Exclusion criteria were: (1) Positive history of pulmonary embolism; (2) history of oxygen-dependent chronic lung disease (COPD); (3) patients who were treated as outpatients and were not hospitalized; and (4) poor image quality of chest CT scan.

3.3. Chest CT Imaging

All clinically suspicious patients underwent chest CT upon admission according to the COVID-19 guidelines (16). The CT scan imaging was obtained in the supine position during end inspiration with a 16-slice scanner (Siemens Somatom emotion CT scanner, Germany). The scanning parameters were as follows: Gantry rotation time of 0.6 seconds, detector array: 16×1.2 , pitch of 1.5, table speed of 150 mm/sec, and a 512×512 matrix. The tube voltage and tube current ranges were 130 kv and 20-345 mA, respectively. A 1.5 mm slice thickness and 1 mm reconstruction interval were used for sagittal and coronal image reconstruction.

Only the initial CT was evaluated in the case of multiple chest CTs. All imaging data were extracted from the picture archiving and communicating system (PACS) and evaluated by 2 experienced radiologists. The parameters were all examined through low-dose CT scans in axial, coronal, and sagittal planes, and the following data were extracted by the radiologist:

The pattern of lung involvement was classified as ground-glass opacification (GGO), consolidation, reticular or mixed. Pulmonary involvement was assessed by using the following system: (1) Upper zone: The area above the carina; (2) middle zone: The area between the carina and inferior pulmonary vein; and (3) lower zone: The region below the inferior pulmonary vein. The amount of pulmonary involvement was scored based on the following system: 0: No involvement, 1: Less than 25%, 2: Between 25 and 50%, 3: Between 51 and 75%, 4: More than 75%. Upper, middle, and lower zonal scores were calculated

by combining the scores of both lungs (maximum score for each zone = 8) and were summed for all three zones to determine the lung total score (maximum score = 24) (3, 17, 18).

A CTR is calculated by dividing the greatest transverse cardiac diameter from outer to outer myocardium by the greatest transverse thoracic diameter from inner to inner chest wall on axial images. The ratio > 0.49 is considered to be an indicator of cardiac enlargement. Moreover, $PA/A > 1$ was defined as PA enlargement and was calculated based on the PA measured within the pulmonary bifurcation to the diameter of the ascending aorta (19).

The IVC diameter was also measured in both anteroposterior and transverse directions at the right diaphragmatic crus, and a diameter > 2 cm is considered significant (20).

To measure the pleural effusion in the CT scan, we divided the anteroposterior (AP) diameter of the chest into quartiles, and the maximum AP diameter was measured at the midclavicular line. Three categories are defined as follows: First AP-quartile effusions are small, second AP-quartile effusions are moderate, and third or fourth AP-quartile effusions are severe. Normal pericardium thickness measured on CT scan is considered to be 2 mm (30 - 50 cc). The effusion depth can estimate the volume of fluid in pericardial space. Therefore, pericardial effusion is reported as small: < 10 mm, moderate: 10 - 20 mm, and large: > 20 mm.

3.4. Statistical Analysis

Data analysis was performed by SPSS v. 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) and the Statistical Package of GraphPad Prism v. 9.3.1.471.

For descriptive statistical analysis, frequencies, percentages, and mean \pm standard deviation (SD) were used. The normal distribution of variables was evaluated by the Shapiro-Wilk test and Kolmogorov-Smirnov test. Age, sex, comorbidities, and other basic variables were adjusted between groups. For comparing groups, Mann-Whitney U, chi-square, and Fisher's exact tests were used. A Cox regression survival analysis was applied to evaluate the effect of cardiac indices on the length of hospitalization, and a logistic regression test was performed to investigate the mortality rate. Moreover, the correlation between lung involvement and cardiac indices was analyzed by linear regression models. P-value < 0.05 was considered statistically significant.

4. Results

4.1. Patient Demographic, Clinical, and Laboratory Findings

A total of 176 patients with COVID-19 were enrolled in the study; 90 patients were male (51.1%) and 86 were female (48.9%) (Table 1). During the follow-up, 121 patients were finally discharged, and 55 patients were deceased. The mean age of participants was 64.9 ± 5.09 years, and the distribution of age ($P = 0.31$) and sex ($P = 0.87$) was equal between the 2 groups. There was no significant difference in the duration of hospitalization between discharged and deceased ($P = 0.36$). Oxygen saturation (SpO_2) level at admission was lower among deaths than discharged patients (86.62 ± 11.3 vs. 9.59 ± 8.09), which was statistically significant ($P < 0.0001$). Among comorbidity factors, the history of diabetes mellitus ($P = 0.0001$), ischemic heart disease, chronic heart failure ($P = 0.0086$), and hypertension (0.034) were significantly more frequent among the deceased. The presence of any comorbidity was also shown to be higher among deceased patients (94.5%) as compared to discharged (71.1%), and this difference was statistically significant ($P = 0.0003$). The laboratory data findings are also summarized in Table 1.

4.2. Association Between Pulmonary and Cardiovascular CCT Parameters and Patient Outcome

Total lung involvement, same as the upper, middle, and lower zones, was significantly more prevalent in deceased patients ($P \leq 0.0001$). The main lung involvement pattern was GGO among all patients (50%), but this was not significantly more frequent in deaths ($P = 0.10$). Consolidation was the second main involvement pattern, which was highly significant in the deceased group in comparison with the discharged ($P = 0.0032$). Bilateral involvement also was found to be more common in COVID-19 patients who died ($P = 0.0005$). Other pulmonary findings that were statistically significant were air bronchogram ($P = 0.0099$) and dilated vessels, which were only found in the deceased group ($P = 0.03$). Moderate and severe pleural effusion varied with 1.7% and 0.8% in recovered patients and 9.1% and 7.3% in patients who died, respectively, which was highly significant ($P = 0.0086$). However, pericardial effusion showed no significant difference between the recovered and the dead ($P = 0.41$). Increased CTR was found in 31.4% of discharged and 50.9% of deceased patients, which was considerable ($P = 0.018$). The $PA/A > 1$ varied by 32.2% in patients who recovered and 52.7% among the deceased, which was statistically significant ($P = 0.012$). The diameter of the trachea was noticeably higher in the deceased group in comparison with the discharged ($P = 0.0042$), but we did

Table 1. Demographic, Clinical, and Laboratory Data Characteristics for Coronavirus Disease 2019 Patients

Variables	Total	Discharged	Deceased	P-Value
Sex				0.87
Male	90 (51.1)	61 (50.4)	29 (52.7)	
Female	86(48.9)	60(49.5)	26(47.2)	
Age (y)	64.9 ± 15.09	64.29 ± 14.91	66.25 ± 15.53	0.31
Duration of hospitalization (days)	9.11± 8.17	8.37± 7.50	10.71 ± 9.35	0.36
SpO₂ (%)	90.03 ± 9.47	91.59 ± 8.09	86.62 ± 11.3	< 0.0001
Comorbidity factors				
Asthma	15 (8.5)	11 (9.1)	4 (7.3)	0.77
Diabetes mellitus	42 (23.9)	14 (11.6)	28 (50.9)	< 0.0001
Ischemic heart disease/congestive heart failure	44 (25)	23 (19)	21 (38.2)	0.0086
Hypertension	90 (51.1)	55 (45.5)	35 (63.6)	0.034
Chronic kidney disease	55 (31.3)	36 (29.8)	19 (34.5)	0.59
Chronic liver disease	7 (4)	4 (3.3)	3 (5.5)	0.68
Presence of any comorbidity	138 (78.4)	86 (71.1)	52 (94.5)	0.0003
Fatty liver	8 (4.6)	4 (3.3)	4 (7.3)	0.26
Ascites	9 (5.1)	3 (2.5)	6 (10.9)	0.027
Laboratory findings				
Leukocyte (× 10 ⁹ /L)	19.91 ± 11.71	20.77 ± 11.22	18.2 ± 12.63	0.035
Platelet (× 10 ⁹ /L)	215.2 ± 110	20.77 ± 11.22	210.5 ± 130.3	0.22
Neutrophil (× 10 ⁹ /L)	74.04 ± 13.94	72.83 ± 14.4	76.79 ± 12.57	0.08
CPK (IU/l)	2 ± 1.74	1.95 ± 1.75	2.09 ± 1.74	0.21
LDH (IU/l)	528.7 ± 342.4	470.4 ± 290.8	655.9 ± 409	0.0003
CRP (mg/L)				0.41
Negative	34 (19.3)	27 (22.3)	7 (12.7)	
+1	43 (24.4)	31 (25.6)	12 (21.8)	
+2	36 (20.5)	24 (19.8)	12 (21.8)	
+3	40 (22.7)	26 (21.5)	14 (25.5)	
+4	23 (13.1)	13 (10.7)	10 (18.2)	

Abbreviations: SpO₂, oxygen saturation; CPK, creatine phosphokinase; LDH, lactate dehydrogenase; CRP, C-reactive protein.

not find a significant difference in IVC diameter between the two groups ($P = 0.07$) (Table 2).

4.3. Odds ratios (OR) of Death and Hazard Ratios (HR) of Hospitalization Based on Cardiovascular CCT Parameters

In the present study, logistic regression analysis was performed to assess the risk of mortality after classifying the age, sex, and comorbidities (Table 3). The odds ratios of death were increased in the CTR > 0.49, PA/A > 1, IVC diameter, pleural effusion, and the amount of lung involvement (OR=1.75, OR=1.99, OR=10.09, OR=10.79, and OR = 1.25, respectively). However, this was only significant in the PA/A > 1 and the volume of lung involvement (P

= 0.046; $P < 0.0001$, respectively). The Cox regression analysis was also performed to investigate the relation between cardiovascular parameters and the time of hospitalization, in which the duration of hospitalization was prolonged along with increased CTR, PA/A > 1, IVC diameter, and pericardial effusion (HR = 1.43, HR = 1.36, HR = 2.22, HR = 1.09, respectively), which was not statistically noticeable. The moderate and severe pleural effusion was significantly associated with prolonged hospitalization (HR = 4.09 and HR = 3.37, respectively; $P = 0.01$ and $P = 0.029$, respectively). Moreover, lung involvement also increased the hospitalization duration considerably (HR = 1.1; $P = 0.0002$).

Table 2. Radiologic Findings of Pulmonary and Cardiovascular Parameters in Chest-Computed Tomography Imaging^a

Variables	Total	Discharged	Deceased	P-Value
Lung involvement				
Total	10.44 ± 6.01	4.26 ± 4.07	6.19 ± 5.54	< 0.0001
Upper zone	1.12 ± 1.95	0.21 ± 0.81	0.5 ± 1.34	0.0001
Middle zone	3.38 ± 3.12	1.30 ± 1.99	1.95 ± 2.58	< 0.0001
Lower zone	5.92 ± 3.10	2.74 ± 2.66	3.74 ± 3.16	< 0.0001
Pattern of involvement				
Ground-glass opacity	88 (50)	55(45.5)	33(60)	0.10
Consolidation	82 (46.6)	47 (38.8)	35 (63.6)	0.0032
Reticular	3 (1.7)	2 (1.7)	1 (1.8)	< 0.99
Mixed	3 (1.7)	2 (1.7)	1 (1.8)	< 0.99
Lesion distribution				
Unilateral	10 (5.7)	8 (6.6)	2 (3.6)	0.72
Bilateral	103 (58.5)	60 (49.6)	43 (78.2)	0.0005
Peripheral	65 (36.9)	43 (35.5)	22 (40)	0.61
Central	34 (19.3)	23 (19)	11 (20)	< 0.99
Both	16 (9.1)	8 (6.6)	8 (14.5)	0.9
Posterior	24 (13.6)	15 (12.4)	9 (16.4)	0.48
Anterior	7 (4)	3 (2.5)	4 (7.3)	0.20
Lateral	9 (5.1)	6 (5)	3 (5.5)	< 0.99
Nonspecific	84 (47.7)	48 (39.7)	36 (65.5)	0.0019
Other findings				
Airway thickening	67 (38.1)	39 (32.2)	28 (50.9)	0.02
Crazy paving	3 (1.7)	1 (0.8)	2 (3.6)	0.23
Lymphadenopathy	72 (40.9)	42 (34.7)	30 (54.5)	0.02
Dilated vessel	3 (1.7)	0 (0)	3 (5.5)	0.03
Airway dilatation	11 (6.3)	5 (4.1)	6 (10.9)	0.1
Air bronchogram	12 (6.8)	4 (3.3)	8 (14.5)	0.0099
Septal thickening	48 (27.3)	29 (24)	19 (34.5)	0.15
Cyst	2 (1.1)	1 (0.8)	1 (1.8)	0.52
Cardiac indices				
Pulmonary artery diameter (mm)	27.89 ± 4.81	27.62 ± 4.95	28.47 ± 4.46	0.10
Aorta diameter (mm)	32.56 ± 4.97	32.63 ± 5.17	32.4 ± 4.53	0.94
Pulmonary artery/aorta ratio	0.86 ± 0.17	0.85 ± 0.17	0.87 ± 0.16	0.24
T/AP inferior vena cava	1.08 ± 0.14	1.06 ± 0.13	1.11 ± 0.15	0.07
T/AP trachea	1.01 ± 0.21	1.04 ± 0.19	0.93 ± 0.23	0.0042
Pleural effusion				
No pleural effusion	110 (62.5)	80 (66.1)	30 (54.5)	0.0086
Mild	54 (30.7)	38 (31.4)	16 (29.1)	
Moderate	7 (4)	2 (1.7)	5 (9.1)	
Severe	5 (2.8)	1 (0.8)	4 (7.3)	
Pericardial effusion				
None	137 (77.8)	95 (78.5)	42 (76.4)	0.41
Mild	36 (20.5)	23 (19)	13 (23.6)	
Moderate	3 (1.7)	3 (2.5)	0 (0)	
Cardiothoracic ratio	66 (37.5)	38 (31.4)	28 (50.9)	0.018
PA/A > 1	68 (38.6)	39 (32.2)	29 (52.7)	0.012

Abbreviations: T/AP, transverse to anteroposterior diameter ratio; PA/A, pulmonary artery to the aorta ratio.

^a Continuous variables are reported as mean ± SD and categorical variables are reported as No. (%).

Table 3. The Hazard Ratio of Hospitalization Time and Odds Ratio of Death Derived from Cardiovascular Computed Tomography Parameters in Patients with Coronavirus Disease 2019

Variables	Odds Ratio (CI 95%)	P-Value	Hazard Ratio	P-Value
CTR > 0.49	1.75 (0.87 - 3.51)	0.11	1.43 (0.82 - 2.51)	0.19
PA/A > 1	1.99 (1.1 - 3.94)	0.046	1.36 (0.79 - 2.34)	0.26
IVC	10.09 (0.90 - 127.3)	0.06	2.22 (0.90 - 127.3)	0.43
Pleural effusion				
Mild	0.72 (0.33 - 1.52)	0.40	1.12 (0.59 - 2.07)	0.71
Moderate	5.35 (1.04 - 42.53)	0.058	4.09 (1.25 - 11.49)	0.01
Severe	10.79 (1.31 - 243.6)	0.052	3.37 (0.96 - 9.14)	0.029
Mild pericardial effusion			1.09 (0.55 - 2.02)	0.77
Lung involvement	1.25 (1.16 - 1.37)	< 0.0001	1.1 (1.04 - 1.16)	0.0002

Abbreviations: CI, confidence interval; CTR, cardio-thoracic ratio; PA/A, pulmonary artery diameter to aorta diameter ratio; IVC, inferior vena cava.

4.4. Association Between Cardiovascular Parameters and Lung Involvement Scores in CCT

The relation between the extent of lung involvement and cardiovascular parameters was investigated with linear regression analysis (Table 4). As shown in Table 4, CTR > 0.49 increased lung involvement in all zones, which was significant in the middle, lower, and total zones ($P < 0.0001$; $P = 0.01$; $P = 0.0002$, respectively). The PA/A > 1 was significantly associated with higher lung involvement in all zones (Table 4). A considerable correlation was also found between The IVC diameter and upper, middle, and total lung scores ($P = 0.0009$; $P = 0.045$; $P = 0.024$ respectively). Moreover, the mild pleural effusion was noticeably associated with zonal involvement in the upper and middle zones ($P = 0.0026$; $P \leq 0.0001$). However, in moderate pleural effusion, the association was observed in lower and total zones ($P = 0.008$; $P = 0.035$), and no correlation was observed between severe pleural effusion and lung involvement except for the upper zone ($P = 0.0327$). The amount of lung involvement was increased in the middle, lower, and total zones in accordance with the first stage of pericardial effusion. However, the severe pericardial effusion showed no correlation with zonal lung involvement.

5. Discussion

Since the beginning of the COVID-19 pandemic in Iran, low-dose CT scans have become a crucial tool for screening and diagnosis of COVID-19 in suspected patients because of the shortage of RT-PCR tests (16, 21). On the other hand, the CT scan has been widely available in Iran, and this fact has made the CT scan a useful alternative to RT-PCR. Moreover, the latest national guideline for the diagnosis and management of COVID-19 patients in Iran suggested

low-dose CT scans besides RT-PCR for the management of all cases with moderate to severe stages of the disease (16). Therefore, low-dose CT scan is now a routine and common part of patient management in COVID-19 centers in Iran. Despite the widespread use of low-dose CT scans in Iran, clinicians still do not take full advantage of them. In this study, we showed how cardiac indices in CT scans of COVID-19 patients can be used for risk stratification and evaluation of the outcomes.

As a result of the COVID-19 relationship with the cardiovascular system, poor outcomes can be experienced in 2 different ways. Previous epidemiological investigations reported that patients with pre-existing cardiovascular disorders such as coronary artery disease, heart failure, and hypertension are at higher risk for adverse outcomes of COVID-19 (22, 23). In our study, comorbidities like hypertension and heart failure were more common in deceased patients. On the other hand, COVID-19, with different mechanisms, causes cardiovascular complications in patients, including acute cardiac injury, heart failure, arrhythmia, myocarditis, acute coronary syndrome, and pleural effusion, which increase the risk of mortality and morbidity (22, 24). In this regard, our results showed that an increase in CTR, PA/A, and IVC diameter raised the likelihood of mortality in COVID-19 patients. Therefore, the findings of the present investigations admitted this two-sided relationship and its importance in predicting the outcomes in COVID-19 patients.

Traditionally, PA/A has been regarded as a reliable indicator of pulmonary hypertension because it correlates with the mean pulmonary artery pressure and predicts poor clinical outcomes in respiratory diseases (25). During the COVID-19 pandemic, several studies reported that increased PA/A is associated with poor prognosis in

Table 4. Association Between Cardiovascular Parameters and Lung Involvement Scores by Linear Regression Analysis in Coronavirus Disease 2019 Patients

Variables	Upper Zone		Middle Zone		Lower Zone		Total Zone	
	Standard Estimation (Standard Error)	P-Value	Standard Estimation (Standard Error)	P-Value	Standard Estimation (Standard Error)	P-Value	Standard Estimation (Standard Error)	P-Value
CTR > 0.49	0.15 (0.22)	0.47	1.76 (0.39)	< 0.0001	1.25 (0.50)	0.01	3.17 (0.84)	0.0002
PA/A > 1	0.42 (0.21)	0.043	0.84 (0.39)	0.033	1.11 (0.48)	0.024	2.37 (0.83)	0.005
IVC	2.34 (0.69)	0.0009	2.69 (1.33)	0.045	1.43 (1.67)	0.39	4.47 (2.83)	0.024
Pleural effusion								
Mild	-0.69 (0.22)	0.0026	1.96 (0.41)	< 0.0001	0.25 (0.53)	0.63	1.53 (0.93)	0.0997
Moderate	-0.33 (0.52)	0.52	1.54 (0.95)	0.11	3.34 (1.24)	0.008	4.54 (2.14)	0.035
Severe	1.27 (0.59)	0.0327	1.41 (1.08)	0.197	-0.78 (1.41)	0.58	1.90 (2.43)	0.43
Pericardial effusion								
Mild	-0.44 (0.25)	0.085	2.36 (0.44)	< 0.0001	1.53 (0.58)	0.009	3.73 (0.99)	0.0002
Moderate	2 (-0.44)	0.57	1.81 (1.35)	0.18	-1.92 (1.80)	0.29	-0.55 (3.05)	0.85

Abbreviations: CTR, cardio-thoracic ratio; PA/A, pulmonary artery diameter to aorta diameter ratio; IVC, inferior vena cava diameter.

patients (3, 26). In a study by Eslami et al. in 2020, PA/A > 1 increased the odds and hazard of death, but it was not significantly correlated with them (3). Another study in Egypt also reported that PA/A > 1 had no significant relationship with the severity of disease in COVID-19 cases (27). A study in Japan found that PA/A > 0.9 was significantly associated with severe respiratory exacerbation and poor prognosis among hospitalized patients (28). Also, Dhok's investigation in India showed PA/A > 0.9 was related to the COVID-19 severity (29). A Turkish study in 2021 found the PA/A > 0.82 as an independent predictor of in-hospital mortality according to the considerable increase in odds of death, while the hazard ratio did not show significant changes (26). In this regard, our study also presented a significant relationship between PA/A > 1 and an increase in the odds ratio of hospitalized death. As it is clear, there is still controversy in accounting PA/A as an independent indicator for the prediction of COVID-19 outcomes in the clinic. One of the main sources for the heterogeneity in findings is using different cut-offs for the PA/A ratio. It seems that the best method for defining the PA/A ratio cut-off is to calculate optimal values in every study according to basic artery diameter in the study population. Also, it is suggested that a meta-analysis be performed in order to draw a conclusion from this controversy. Considering the high PA/A ratio can indicate pulmonary hypertension and microvascular thrombi is the leading cause, determining the ratio is important clinically, as it allows clinicians to assess patients who might benefit from early management of pulmonary hypertension and

conduct cardiac echocardiography and anticoagulant therapy.

A CTR > 0.5 indicates heart enlargement and is used as a prognostic factor in different disorders, such as respiratory and cardiac diseases (30). Due to COVID-19's multi-organ nature and the fact that it affects both the heart and lungs, it was expected that CTR would change among the patients. Some investigations from different parts of the world showed that cardiomegaly was associated with disease severity (3, 31). In Kanayama et al.'s study in Japan, cardiomegaly was found to be strongly associated with the severity of the disease on admission (31). An Iranian study also reported that cardiomegaly showed significant relationships with odds and hazard of death among hospitalized patients (3). Also, Truskiewicz et al.'s study in Poland found that CTR can be a useful prognosis predictor of right ventricle enlargement in COVID-19 patients with suspected pulmonary embolism (2). On the other hand, some reports indicate that cardiomegaly was not related to an increase in the risk of adverse outcomes in COVID-19 cases. In a study by Khosravi et al. (32), cardiomegaly was more common in deceased cases, but it did not show a significant association with worse outcomes. In addition, although our findings showed more frequency of cardiomegaly in deceased patients, it did not have significant relationships with an increase in odds and hazard of death. As there are different results on both sides, CTR > 0.5 cannot be accounted as a prognostic factor for COVID-19 yet. Therefore, more evidence and investigations are needed to determine cardiomegaly's role in predicting the COVID-19

prognosis.

The present study faced some limitations that need to be mentioned for improvement of future studies. First, only the images of CT scans of the patients on admission were used for analysis. It is suggested that the changes in cardiac indices in serial imaging be considered in future studies. Second, the thoracic motion and respiratory changes were not controlled and evaluated in the study, which may influence some measurements of indices. Third, we did not evaluate normal values of ratios in our study and used defined cut-offs. The cut-offs of ratios according to the normal features of the study population should be determined.

In conclusion, cardiac indices in chest CT of COVID-19 patients can be accounted for in the prediction of patient outcomes, such as PA/A > 1 ratio, which increases the likelihood of in-hospital death. Considering the controversy about the findings for suggesting CT-measured cardiac indices as prognostic factors in COVID-19 patients, further primary and secondary studies are needed.

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Footnotes

Authors' Contribution: SL, study concept and design, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, study supervision; MS, acquisition of data, drafting of the manuscript, administrative, technical, and material support, analysis and interpretation of data; F.H, drafting of the manuscript, critical revision of the manuscript for important intellectual content, analysis and interpretation of data, administrative, technical, and material support; MM, statistical analysis, drafting of the manuscript, acquisition of data, administrative, technical, and material support.

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Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to limitations on having access to online databases.

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References

- Esakandari H, Nabi-Afjadi M, Fakkari-Afjadi J, Farahmandian N, Miresmaeili SM, Bahreini E. A comprehensive review of COVID-19 characteristics. *Biol Proced Online*. 2020;22:19. [PubMed ID: 32774178]. [PubMed Central ID: PMC7402395]. <https://doi.org/10.1186/s12575-020-00128-2>.
- Truszkiewicz K, Poreba M, Poreba R, Gac P. Radiological Cardiothoracic Ratio as a Potential Predictor of Right Ventricular Enlargement in Patients with Suspected Pulmonary Embolism Due to COVID-19. *J Clin Med*. 2021;10(23). [PubMed ID: 34884405]. [PubMed Central ID: PMC8658615]. <https://doi.org/10.3390/jcm10235703>.
- Eslami V, Abrishami A, Zarei E, Khalili N, Baharvand Z, Sanei-Taheri M. The Association of CT-measured Cardiac Indices with Lung Involvement and Clinical Outcome in Patients with COVID-19. *Acad Radiol*. 2021;28(1):8-17. [PubMed ID: 33041195]. [PubMed Central ID: PMC7528899]. <https://doi.org/10.1016/j.acra.2020.09.012>.
- Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):811-8. [PubMed ID: 32219356]. [PubMed Central ID: PMC7101506]. <https://doi.org/10.1001/jamacardio.2020.1017>.
- Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5(7):802-10. [PubMed ID: 32211816]. [PubMed Central ID: PMC7097841]. <https://doi.org/10.1001/jamacardio.2020.0950>.
- Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nat Rev Cardiol*. 2020;17(9):543-58. [PubMed ID: 32690910]. [PubMed Central ID: PMC7370876]. <https://doi.org/10.1038/s41569-020-0413-9>.
- Bohm M, Frey N, Giannitsis E, Sliwa K, Zeiher AM. Coronavirus Disease 2019 (COVID-19) and its implications for cardiovascular care: expert document from the German Cardiac Society and the World Heart Federation. *Clin Res Cardiol*. 2020;109(12):1446-59. [PubMed ID: 32462267]. [PubMed Central ID: PMC7252421]. <https://doi.org/10.1007/s00392-020-01656-3>.
- Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, et al. COVID-19 and Cardiovascular Disease. *Circulation*. 2020;141(20):1648-55. [PubMed ID: 32200663]. <https://doi.org/10.1161/CIRCULATIONAHA.120.046941>.
- Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. *Features, Evaluation, and Treatment of Coronavirus (COVID-19)*. Treasure Island (FL): StatPearls; 2024.

10. Kayahan Ulu EM, Terzi Ö. CT Measured Cardiovascular and Metabolic Risk Factors in Patients with COVID-19 Infections. *Turk J Intensive Care*. 2022;**20**(1):39-47. <https://doi.org/10.4274/tybd.galenos.2022.18199>.
11. Karam M, Althuwaikh S, Alazemi M, Abul A, Hayre A, Alsaif A, et al. Chest CT versus RT-PCR for the detection of COVID-19: systematic review and meta-analysis of comparative studies. *JRSM Open*. 2021;**12**(5):20542704211011800. [PubMed ID: 34035931]. [PubMed Central ID: PMC8127597]. <https://doi.org/10.1177/20542704211011837>.
12. Wingate-Samuels L, Javaid J, Chambers J. Echocardiography is not indicated for an enlarged cardiothoracic ratio. *Br J Cardiol*. 2013;**20**(4):149-50. <https://doi.org/10.5837/bjc.2013.30>.
13. Zouk AN, Gulati S, Xing D, Wille KM, Rowe SM, Wells JM. Pulmonary artery enlargement is associated with pulmonary hypertension and decreased survival in severe cystic fibrosis: A cohort study. *PLoS One*. 2020;**15**(2). e0229173. [PubMed ID: 32078644]. [PubMed Central ID: PMC7032721]. <https://doi.org/10.1371/journal.pone.0229173>.
14. Ogata H, Kumasawa J, Fukuma S, Mizobuchi M, Kinugasa E, Fukagawa M, et al. The cardiothoracic ratio and all-cause and cardiovascular disease mortality in patients undergoing maintenance hemodialysis: results of the MBD-5D study. *Clin Exp Nephrol*. 2017;**21**(5):797-806. <https://doi.org/10.1007/s10157-017-1380-2>.
15. Okute Y, Shoji T, Hayashi T, Kuwamura Y, Sonoda M, Mori K, et al. Cardiothoracic Ratio as a Predictor of Cardiovascular Events in a Cohort of Hemodialysis Patients. *J Atheroscler Thromb*. 2017;**24**(4):412-21. [PubMed ID: 27629255]. [PubMed Central ID: PMC5392479]. <https://doi.org/10.5551/jat.36426>.
16. Mahdavi A, Khalili N, Davarpanah AH, Faghihi T, Mahdavi A, Haseli S, et al. Radiologic Management of COVID-19: Preliminary Experience of the Iranian Society of Radiology COVID-19 Consultant Group (ISRCC). *Iran J Radiol*. 2020;**17**(2). <https://doi.org/10.5812/iranjradiol.102324>.
17. Abrishami A, Khalili N, Dalili N, Khaleghnejad Tabari R, Farjad R, Samavat S, et al. Clinical and Radiologic Characteristics of COVID-19 in Patients With CKD. *Iran J Kidney Dis*. 2020;**14**(4):267-77. [PubMed ID: 32655021].
18. Mousa M, Matar M, Matar M, Jaber S, Jaber FS, Al Ajerami Y, et al. Role of cardiovascular computed tomography parameters and lungs findings in predicting severe COVID-19 patients: a single-centre retrospective study. *Egyptian Journal of Radiology and Nuclear Medicine*. 2022;**53**(1). <https://doi.org/10.1186/s43055-022-00910-0>.
19. Gollub MJ, Panu N, Delaney H, Sohn M, Zheng J, Moskowitz CS, et al. Shall we report cardiomegaly at routine computed tomography of the chest? *J Comput Assist Tomogr*. 2012;**36**(1):67-71. [PubMed ID: 22261772]. <https://doi.org/10.1097/RCT.0b013e318241e585>.
20. Nath J, Vacek JL, Heidenreich PA. A dilated inferior vena cava is a marker of poor survival. *Am Heart J*. 2006;**151**(3):730-5. [PubMed ID: 16504642]. <https://doi.org/10.1016/j.ahj.2005.04.023>.
21. Isapanah Amlashi F, Gilani N, Besharat S. Does Local or National Quarantine May Save More Lives in Iran during COVID-19 Epidemic? *Iran J Public Health*. 2020;**49**(Suppl 1):125-6. [PubMed ID: 34268219]. [PubMed Central ID: PMC8266005]. <https://doi.org/10.18502/ijph.v49iS1.3683>.
22. Shafi AMA, Shaikh SA, Shirke MM, Iddawela S, Harky A. Cardiac manifestations in COVID-19 patients-A systematic review. *J Card Surg*. 2020;**35**(8):1988-2008. [PubMed ID: 32652713]. [PubMed Central ID: PMC7404674]. <https://doi.org/10.1111/jocs.14808>.
23. Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and Multiorgan Response. *Curr Probl Cardiol*. 2020;**45**(8):100618. [PubMed ID: 32439197]. [PubMed Central ID: PMC7187881]. <https://doi.org/10.1016/j.cpcardiol.2020.100618>.
24. Bansal M. Cardiovascular disease and COVID-19. *Diabetes Metab Syndr*. 2020;**14**(3):247-50. [PubMed ID: 32247212]. [PubMed Central ID: PMC7102662]. <https://doi.org/10.1016/j.dsx.2020.03.013>.
25. Terzikhan N, Bos D, Lahousse L, Wolff L, Verhamme KMC, Leening MJG, et al. Pulmonary artery to aorta ratio and risk of all-cause mortality in the general population: the Rotterdam Study. *Eur Respir J*. 2017;**49**(6). [PubMed ID: 28619955]. <https://doi.org/10.1183/13993003.02168-2016>.
26. Erdogan M, Ozturk S, Erdol MA, Kasapkara A, Besler MS, Kayaaslan B, et al. Prognostic utility of pulmonary artery and ascending aorta diameters derived from computed tomography in COVID-19 patients. *Echocardiography*. 2021;**38**(9):1543-51. [PubMed ID: 34355824]. [PubMed Central ID: PMC8444889]. <https://doi.org/10.1111/echo.15170>.
27. Abosamak MF, Henry BM, Aly MF, Lavie CJ, Sanchis-Gomar F. CT-Determined Maximum Pulmonary Artery to Ascending Aorta Diameter Ratio in Nonsevere COVID-19 Patients. *Acad Radiol*. 2021;**28**(3):440-1. [PubMed ID: 33478887]. [PubMed Central ID: PMC7834716]. <https://doi.org/10.1016/j.acra.2020.12.023>.
28. Hayama H, Ishikane M, Sato R, Kanda K, Kinoshita N, Izumi S, et al. Association of plain computed tomography-determined pulmonary artery-to-aorta ratio with clinical severity of coronavirus disease 2019. *Pulm Circ*. 2020;**10**(4):2045894020969490. [PubMed ID: 33282198]. [PubMed Central ID: PMC7686624]. <https://doi.org/10.1177/2045894020969492>.
29. Dhok AP, Dhawan S, Chajjed RM, Mitra K. CT derived pulmonary vascular indices and severity of pneumonia in Covid-19 patients: A retrospective study. *Med Sci*. 2022;**26**(124):1-9. <https://doi.org/10.54905/disssi/v26i124/ms218e2079>.
30. Truszkiewicz K, Poreba R, Gac P. Radiological Cardiothoracic Ratio in Evidence-Based Medicine. *J Clin Med*. 2021;**10**(9). [PubMed ID: 34066783]. [PubMed Central ID: PMC8125954]. <https://doi.org/10.3390/jcm10092016>.
31. Kanayama A, Tsuchihashi Y, Otomi Y, Enomoto H, Arima Y, Takahashi T, et al. Association of severe COVID-19 outcomes with radiological scoring and cardiomegaly: findings from the COVID-19 inpatients database, Japan. *Jpn J Radiol*. 2022;**40**(11):1138-47. [PubMed ID: 35881259]. [PubMed Central ID: PMC9315080]. <https://doi.org/10.1007/s11604-022-01300-2>.
32. Khosravi B, Aghaghazvini L, Sorouri M, Naybandi Atashi S, Abdollahi M, Mojtavani H, et al. Predictive value of initial CT scan for various adverse outcomes in patients with COVID-19 pneumonia. *Heart Lung*. 2021;**50**(1):13-20. [PubMed ID: 33097297]. [PubMed Central ID: PMC7556824]. <https://doi.org/10.1016/j.hrtlng.2020.10.005>.