Original Article

Prognostic utility of cardiovascular indices in COVID-19 infection: A single-center prospective study in India

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Abstract

Background: Cardiac signs can show illness progression and severity in a number of respiratory and cardiovascular disorders. The possible importance of CT findings in the prognosis and result of COVID-19 patients is related to the severity of lung disease and cardiac parameters. The CT-assessed cardiac indices are known for predicting the involvement of extent of diseases. Hence, the objective of this study was to correlate the extent of cardiovascular and respiratory involvement in predicting the severity of disease using CT-assessed cardiac indices in Indian population suffering from COVID-19. **Methodology:** A total of 120 COVID-19 patients were included following the inclusion criteria for one year. The confounding factors were assessed and analyzed. The correlation between the cumulative hazard function of death and duration in hospital along with survival rate were done in terms of pulmonary artery-to-aorta ratio (PA/A), and cardiothoracic ratio (CTR). **Results:** The analysis showed mean age of patients to be 49.5(±15.32) years in which mean females were 38(±31.7) and males were 82(±68.3). The interquartile range of CT severity was 8. The PA/A ratio in discharged patients was 0.85 when compared to deceased patients with 1.03 having statistically significant inference ($P = 0.00$). The CTR ($P = 0.00$), epicardial adipose thickness ($P = 0.00$), epicardial adipose density ($P = 0.00$), and D-dimer ($P = 0.007$) were showing statistically significant inference. **Conclusion:** The predictive values of CT-assessed cardiac indices might be used for predicting the involvement of cardiovascular and respiratory involvement in COVID-19 patients. It could have an impact on improving the possibilities of survival of patients suffering from COVID-19 in India.

Keywords: Cardiac indices, computed tomography, COVID-19, SARS-CoV-2

Introduction

Developing countries have witnessed a rising level of viruses which represented itself as a major concern worldwide during the pandemic.[1] The coronavirus disease 2019 (COVID-19) is a complicated viral condition that impacts the lungs.[2] COVID-19 was first discovered in humans in December 2019 by researchers in Wuhan, China.[3] On 30 January 2020, the World Health Organization (WHO) designated COVID-19 a global pandemic. Timely identification of patients with critical illnesses should lead to more efficient regression testing and precedence of rising patients' healthcare coverage.[2]

While the majority of COVID-19 patients have a moderate form of the disease, a small percentage develop fast pneumonia, along with coronavirus-induced severe acute respiratory syndrome and Middle East respiratory syndrome; acute respiratory distress syndrome (ARDS) can also be caused by COVID-19.[4] Throughout the diagnosis and monitoring of lung disorders, mainly pneumonia,

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computed tomography (CT) of the chest is an important and useful method.[5] COVID-19 chest imaging data was mainly introduced in January 2020, and the majority of hospitalized patients had bilateral lung fibrosis and ground glass nodules.[3]

A worldwide expert recommendation on the use of lung radiography in various health settings was published by the Fleischer association.[6] For patients with suspected COVID-19, the Society of Thoracic Radiology, the American College of Radiology, and the Radiological Society of North America has provided updated recommendations on the use of plain chest radiography and CT imaging. These guidelines indicate a good clinical skill against evaluating chest CT imaging to diagnose COVID-19 on a regular basis because the symptoms are described as non-specific and normal CT imaging findings would be unable to screen out the infection.[7] In a range of conditions and diseases, imaging-based cardiac parameters have been demonstrated to indicate an increased risk of morbidity and death.

An increased cardiothoracic ratio (CTR) or pulmonary artery-to-aorta (PA/A) ratio, for example, has been associated with a poor prognosis in individuals with respiratory disorders; such indices could also indicate an increased risk of cardiovascular disease (CVD). Ground-glass opacity (GGO), consolidation with air bronchogram, interlobular septal thickening, centrilobular nodule, and reticular opacities analytical techniques to continuously monitor lung problems in chest CT images of patients were documented previously.[8] Various cardiac characteristics, including greater epicardial adipose tissue (EAT) thickness, reduced EAT density, particularly dilated inferior vena cava (IVC), also can help to determine significant CVD and respiratory episodes. The aim of the research provides information to CT predictive variables of cardiac indices determining clinical outcome in COVID-19 patients. Cardiac signs can show illness progression and severity in a number of respiratory and cardiovascular disorders. The possible importance of CT findings in the prognosis and result of COVID-19 patients is related to the severity of lung disease and cardiac parameters. The CT-assessed cardiac indices are known for predicting the involvement of extent disease. Hence, the objective of this study is to correlate the extent of cardiovascular and respiratory involvement in predicting the severity of disease using CT-assessed cardiac indices in Indian population suffering from COVID-19.

Materials and Methods

The study was accepted by the Institutional Ethical Review Committee with reference number NKPSIMS & RC and LMH/IEC-Pharmacology/26/2020. The duration of the study was April 2020 to March 2021. All participants who enrolled in the research signed a written informed consent before initiating the study. Participants with a confirmed diagnosis of COVID-19 were hospitalized in our academic tertiary care center for the correlational study. Inclusion criteria included diagnosed case of COVID-19 with nasopharyngeal swab sample using real-time reverse transcriptase polymerase chain reaction (RTPCR) assay, CT-imaging of chest predicting pneumonic COVID-19, and participants above 21 years of age. History of pulmonary emboli, COPD with oxygen dependency, patients treated on output basis, and low and unsatisfactory imaging quality due to serious cardiac motion disturbance were excluded from the allotment of the samples. At the time of enrollment, participant's demographic and medical information were obtained. To confirm the past medical history and existence of comorbidities, laboratory testing, and current symptoms with signs; a pre-designed questionnaire was filled out. The participant's initial chest CT scan's radiological findings have also been recorded.

CT Scanning of the chest

The Fleischer Society published a consensus on the role of chest imaging (primarily CT scan) in clinical outcomes during the COVID-19 pandemic, discussing various clinical scenarios such as the severity of respiratory disease, pre-test possibility, specific disease comorbidities, and important inadequate capacity.[9] All clinically diagnosed patients got a low-dose non-enhanced chest CT upon admission, as per national COVID-19 guidelines.[10] Only the first CT was investigated in patients who had more than one CT. Every patient had a CT scan in the supine position during end-inspiration with a Toshiba Activion 16, 16 slice helical MDCT scan machine. The following scan parameters were used for a low-dose CT protocol: Table speed of 45.2 mm/rotation, 20 mAs, 120 kVp, and a 300 £ 300 matrix [Figure 1]. Gantry rotation duration of 0.5 seconds, 0.625 mm £ 16-detector array, pitch of 1.4, 0.625 mm £ 16-detector array, pitch of 1.4, 0.625 mm £ 16-detector array, pitch of 1.4, table speed of 45.2 mm/rotation, 20 mAs. For sagittal and coronal image reconstruction, 1 mm slice thickness and 1 mm reconstruction interval were utilised as shown in Figure 1. After each CT, the machines were disinfected with ethanol and didecyl-dimethylammonium chloride (DDAC), and passive air ventilation was performed for at least 30 minutes.

Statistical analysis

The statistical analysis followed mean with standard deviation in normal continuous distribution and median in skewed continuous distribution. The frequencies were analyzed categorically in percentages and by using Chi-squared test. Mann–Whitney *U*

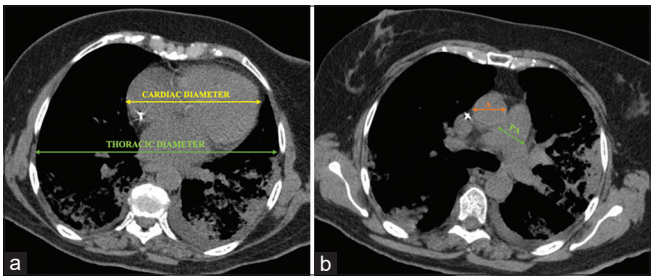

Figure 1: (a and b) Axial images of chest computed tomography (CT) showing measurement of cardiac indices. (a) CT-derived cardiothoracic ratio: The yellow arrow depicts the greatest transverse cardiac diameter and the green arrow indicates the greatest transverse thoracic diameter; (b) CT-derived pulmonary artery (green arrow)-to-aorta (orange arrow) ratio (PA/A)

test and independent *t* test were applied for comparing normal and skewed data of discharged and deceased patients. The Cox regression and logistic regression were used for analysis of survival as per the indices of cardia impacting the outcome of the patient. In the Cox regression model, discharge or death of patient were the outcome and the duration of hospital stay was the duration of outcome. The regression pattern of linear model was used for determining the relationship between the cardiac size and involvement of lung variable where the cardiac variables were placed as dependent variables. Linear regression as well as logistic regression were analyzed with the adjusted values of the participant's age, gender, and comorbid factors. A *P* value of less than 0.05 was termed as statistically significant. Statistical Package for the Social Sciences (SPSS) v. 27.0 was used for the entire statical analysis of the variables.

Results

One hundred twenty COVID-19 positive patients were recruited as per the inclusion and exclusion criteria. The exemplar confounding details with imaging findings and severity of CT score along with cardiac indices of individual participants were included in Table 1. Mean age was 49.50 ± 15.32 years old, out of which 82 (68.3) were male. The deceased and discharged patients followed equal distribution of age. Following the follow-up, 23 patients of 120 were deceased and 97 were discharged. The deceased COVID-19 patients were significantly showing the median length of hospitalization.

The analysis of CT severity score was highly significant ($P = 0.000$) which was done with interquartile range of median and was 7 in discharged patients and 18 in deceased patients. The normal, mild, moderate and severe distribution were 32 (33), 25 (25.8), 28 (28.9) and 12 (12.4) in discharged patients, whereas 0, 4 (17.4), 5 (21.7) and 14 (60.9) in deceased patients, respectively.

Cardiac indices

The pulmonary artery diameter was varied with 26.44 ± 2.26 in discharged patients and 29.41 ± 2.76 in deceased patients with $P = 0.00$ stating it highly significant. The aorta diameter was analyzed as 30.94 ± 2.71 in discharged patients and 29.44 ± 1.56 in deceased patients with significant affection ($P = 0.012$). The PA/A in discharged patients was 0.85 as compared to deceased patients with 1.03, having statistically significant inference ($P = 0.00$). The CTR ($P = 0.00$), epicardial adipose thickness ($P = 0.00$), epicardial adipose density ($P = 0.00$), and D-dimer ($P = 0.007$) were showing statistically significant inference; however T/AP trachea ($P = 0.176$) had shown insignificant variation.

The certainty of deceased patients with PA/A more than 1 was 24% as compared to 16% in discharged patients. However, the probability of PA/A of deceased patients being ≤1 was 96% as compared to discharged patient, which was 7%. CTR ≥0.49 was 21% and 66% in discharged and deceased patients, respectively. However, the CTR less than 0.49 was 54% in deceased patients as compared to 2% in discharged patients as shown in Table 2.

The "discharge or death" of patient were considered as the outcome and the "duration of hospital stay" as duration of event; the impact of PA/A and CTR were evaluated on the number of patients deceased in hospital stay duration. In cox

Table 1: Patient's baseline demographic characteristics and CT imaging details. Mean was tested using independent *t*-test and median was tested using Mann-Whitney *U* test. Chi-squared test was used for categorical distribution of data

Characteristic	Total (*n*=120)	Discharged (*n*=97)	Deceased (*n*=23)	Statistical significance (*P*)
Demographics				
Mean age	49.50±15.32	48.08±16.19	55.48±8.94	0.037
Sex				
Male	82 (68.3)	67 (69.1)	15 (65.2)	0.721
Female	38 (31.7)	30 (30.9)	08 (34.8)	
Imaging findings				
CT severity score (Median [Inter-quartile range])	8 (0-15)	7 (0-12)	18 (11-20)	0.000
Severity based on CT score				
Normal	32 (26.7)	32 (33.0)	0 (0.00)	
Mild	29 (24.2)	25 (25.8)	04 (17.4)	
Moderate	33 (27.5)	28 (28.9)	05 (21.7)	
Severe	26 (21.7)	12 (12.4)	14 (60.9)	0.000
Cardiac indices				
Pulmonary artery diameter (mm)	27.01±2.63	26.44±2.26	29.41±2.76	0.000
Aorta diameter (mm)	30.66±2.59	30.94±2.71	29.44±1.56	0.012
Pulmonary artery/aorta	0.86 (0.83-0.90)	0.85 (0.82-0.88)	1.03 (0.99-1.10)	0.000
Cardiothoracic ratio (CTR)	0.50 (0.47-0.55)	0.48 (0.46-0.52)	0.56 (0.54-0.58)	0.000
Epicardial adipose thickness (mm)	6.60 (6.40-6.80)	6.50 (6.40-6.70)	7.80 (7.30-8.00)	0.000
Epicardial adipose density (mm)	−97.00 (−99.75-[−94.00])	−96.00 (−97.00-[−92.00])	−111.00 (−118.00-−108.00])	0.000
T/AP trachea	1.12 (1.11-1.13)	1.12 (1.11-1.13)	1.12 (1.11-1.13)	0.176
D-dimer	0.45 (0.28-2.34)	0.39 (0.27-2.00)	2.32 (0.41-2.78)	0.007

adjusted models, CTR ≥0.49 showed significant hazardous effect of death (hazard ratio [HR] = 11.4, $P = 0.006$). This implication was contrasted by insignificant PA/A (HR = 1.35, $P = 0.63$). Figure 2 shows the correlation of cumulative hazard function of death and duration in hospital with CTR. However, Figure 3 demonstrates the correlation of cumulative survival functions of death and duration in hospital with PA/A. Figure 4 shows the correlation of CT ratio and outcome and Figure 5 shows the correlation of PA/A ratio and outcome.

Discussion

Application of diagnostic imaging has been augmented into clinical practice assisting the assessment and appropriate management of the disease. However, many of the studies integrate findings such as CT to grade the severity of the disease.[11] A recent study conducted in New York on 105 patients who were suffering from COVID-19 depicted right ventricular hypertrophy during hospitalization; 31% of the enrolled subjects showed dilated right ventricle; periodic echocardiography was used to measure the ventricular size dilation.[12,13] Our results showed that the involvement of the lung is more in the individuals with higher CT score. We also evaluated the individuals on the CT imaging report and the reports showed the involvement of bilateral lungs.[14] Latest study showed that the periodic CT scan has shown significant similarity with X-ray ($r = 0.802$).[15]

As per the literature available, the severity in terms of clinical signs is correlated with the involvement of lungs for patients suffering from COVID-19.[13] This study assessed the impact of cardiac indices in terms of CTR and PA/A ratio and confirmed the findings in India. It was found to be significant in patients who were deceased as compared to those who were discharged. We also assessed the extent of lung involvement and found increased CT score in patients suffering from COVID-19 suggesting increased PA/A ratio and CT ratio and indicating an immediate care response for cardiovascular and respiratory involving risk factors.

Assessing the parameters evaluating the risk factors has been in trend since decades, but using it in determining the extent

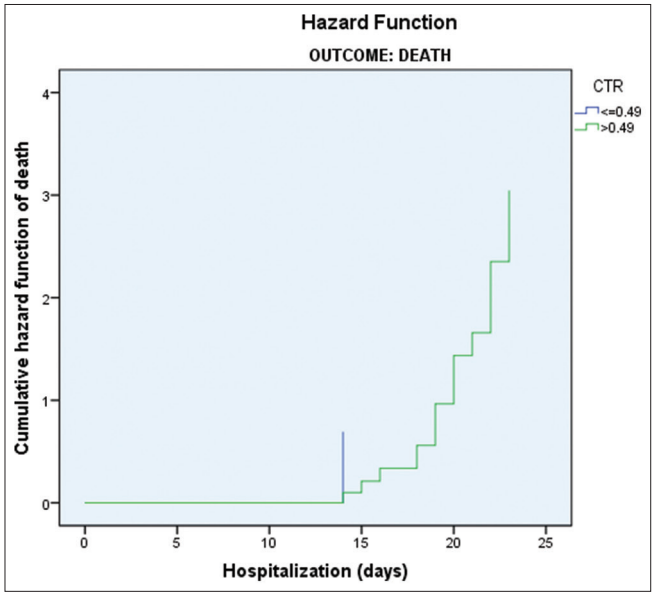

Figure 2: Correlation of cumulative hazard function of death and duration in hospital with CTR

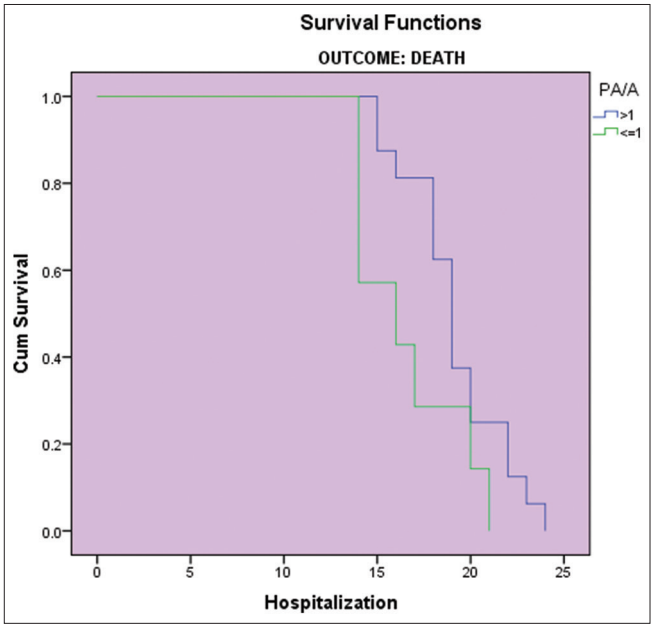

Figure 3: Correlation of cumulative survival functions of death and duration in hospital with PA/A

Table 2: Predictors of cardiac indices affecting clinical outcome in patients with COVID-19 - Logistic regression model and Cox model

Characteristic	Discharged (%) (*n*=97)	Death (%) (*n*=23)	Total (%) (*n*=120)	Logistic model*		Cox model*	
				Adjusted Odds Ratio (95% CI)	*P*	Hazard Ratio (95% CI)	*P*
PA/Aorta							
> 1	08 (33.3)	16 (66.7)	24 (100)	19.35 (5.77-64.89)	0.000	1.37 (0.46-4.06)	0.561
≤ 1	89 (92.7)	07 (7.3)	96 (100)	Reference		Reference	
CTR							
≥ 0.49	45 (68.2)	21 (31.8)	66 (100)	8.04 (1.55-41.48)	0.013	0.23 (0.04-1.31)	0.098
< 0.49	52 (96.3)	02 (3.7)	54 (100)				

*Adjusted for age and sex

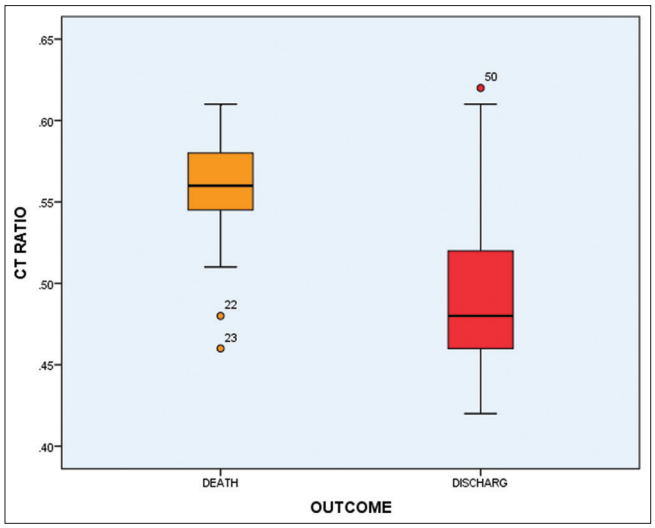

Figure 4: Correlation of CT ratio and outcome

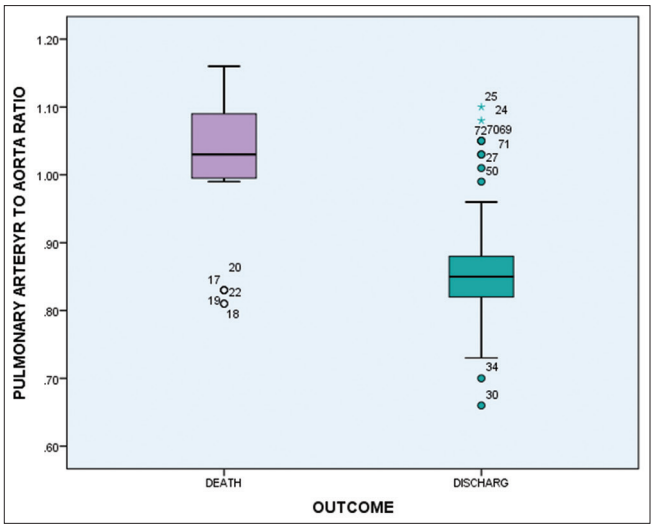

Figure 5: Correlation of PA/A ratio and outcome

of involvement of cardiovascular and respiratory risk factors predicted on the survival rate of patients suffering from COVID-19.[16] A study in Wuhan found longitudinal strain on ventricles of right side on echocardiography and reported an independent impact on determining the survival rate of patients suffering from COVID-19.[17] However, determining the survival rate with PA/A ratio suggested an insignificant determination of death rate in patients with PA/A >1, which is previously known as a marker in determining pulmonary hypertension.[18] A similar study was also done on 45 COVID-19 patients in which they commented that the survival rate was significantly low in patients with increased PA which was not linked to alteration in PA/A ratio.[19]

Conclusion

The predictive values of CT-assessed cardiac indices might be used for predicting the involvement of cardiovascular and respiratory involvement in COVID-19 patients. It could have a prognostic on improving the possibilities of survival rate of patients suffering from COVID-19 in India.

Study limitation

The literature commenting on the prognosis of cardiovascular diseases in relation to the epicardial adipose tissue thickness and cardiothoracic ratio are limited. The sample size for determining the impact of cardiac indices on survival rate of patients suffering from COVID-19 in India was small in our study and can be assessed on larger sample size. Also, the duration of the study can be increased to see the extent of impact of cardiac indices.

Author's contribution

All authors contributed equally to the manuscript.

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We thank the patients who participated and contributed samples to the study.

Informed consent

Written informed consent was obtained from all individual participants included in the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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