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Utility of visual coronary artery calcification on non-cardiac gated thoracic CT in predicting clinical severity and outcome in COVID-19[☆]

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ABSTRACT

Background: Assessment of visual-coronary artery calcification on non-cardiac gated CT in COVID-19 patients could provide an objective approach to rapidly identify and triage clinically severe patients for early hospital admission to avert worse prognosis.
Purpose: To ascertain the role of semi-quantitative scoring in visual-coronary artery calcification score (V-CACS) for predicting the clinical severity and outcome in patients with COVID-19.
Materials and methods: With institutional review board approval this study included 67 COVID-19 confirmed patients who underwent non-cardiac gated CT chest in an inpatient setting. Two blinded radiologist (Radiologist-1 &2) assessed the V-CACS, CT Chest severity score (CT-SS). The clinical data including the requirement for oxygen support, assisted ventilation, ICU admission and outcome was assessed, and patients were clinically subdivided depending on clinical severity. Logistic regression analyses were performed to identify independent predictors. ROC curves analysis is performed for the assessment of performance and Pearson correlation were performed to looks for the associations.
Results: V-CACS cut off value of 3 (82.67% sensitivity and 54.55% specificity; AUC 0.75) and CT-SS with a cut off value of 21.5 (95.7% sensitivity and 63.6% specificity; AUC 0.87) are independent predictors for clinical severity and also the need for ICU admission or assisted ventilation. The pooling of both CT-SS and V-CACS (82.67% sensitivity and 86.4% specificity; AUC 0.92) are more reliable in terms of predicting the primary outcome of COVID-19 patients. On regression analysis, V-CACS and CT-SS are individual independent predictors of clinical severity in COVID-19 (Odds ratio, 1.72; 95% CI, 0.99–2.98; $p = 0.05$ and Odds ratio, 1.22; 95% CI, 1.08–1.39; $p = 0.001$ respectively). The area under the curve (AUC) for pooled V-CACS and CT-SS was 0.96 (95% CI 0.84–0.98) which correctly predicted 82.1% cases.
Conclusion: Logistic regression model using pooled Visual-Coronary artery calcification score and CT Chest severity score in non-cardiac gated CT can predict clinical severity and outcome in patients with COVID-19.

1. Introduction

Corona Virus disease (COVID-19) is a viral infectious disease caused by a novel strain of the corona virus primarily causing pulmonary syndrome.[1] Its origin was reported in a cluster of patients in Wuhan city of Hubei Province, China. Due to a higher viral reproduction number and infectious nature of the disease, the virus transmitted rapidly out of China with WHO subsequently declaring this as a global pandemic. Despite quarantine rules and travel restrictions it has been difficult to contain the spread of COVID-19. Rapid testing and early identification are essential to diagnose and mitigate the spread of the disease.

The understanding of COVID-19 pathophysiology in relation to

Abbreviations: V-CACS, Visual Coronary artery calcification Score; CT-SS, CT Chest Severity Score; COVID-19, Corona Virus disease-2019; RT-PCR, Reverse Transcriptase Polymerase chain reaction.; ECMO, Extracorporeal membrane oxygenation.

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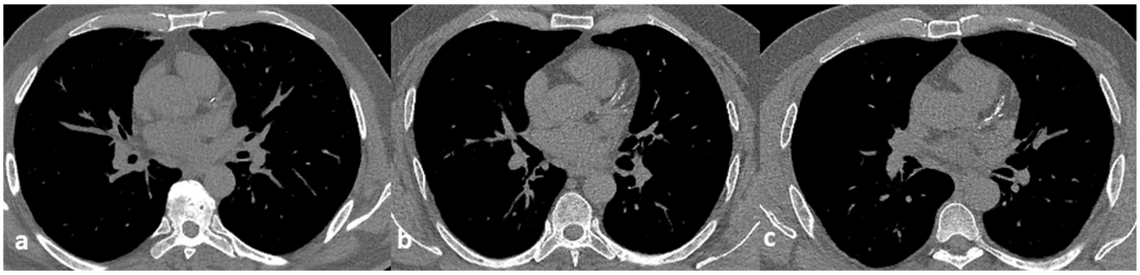

Fig. 1. V-CACS in CT scan, (a) Mild calcification, score-1; (b) Moderate calcification, score-2; (c) Severe calcification, score-3.

radiological behavior is growing day by day. The typical CT chest findings in COVID-19 include groundglass opacities, with or without consolidations and reticulations on lung region close to the visceral pleural surface with a posterior predominant and multifocal distributions.[5–10] The reported specificity of CT scan is reportedly moderate to low, it is reported between 25 and 56%.[11,12,14,15] The low reported sensitivity is because the CT features might overlap between COVID-19 and other RNA viral pneumonia like Respiratory Syncytial Virus (RSV) and Human Para influenza virus (HPIV).[16,17] Due to low specificity of CT chest the American College of Radiology discourages its systemic use for diagnosing COVID-19.[18] Recently researchers have proposed a scoring system with a cut-off value based on CT chest assessment that correlates to clinical severity.[2] This pulmonary inflammation load score was seen to be higher in patients with clinically severe COVID-19 compared to patients with clinically mild disease. Mild cases require symptomatic treatment, while severe cases require intensive care unit admission and continuous monitoring.

Coronary artery calcification is a marker of atherosclerotic plaque and thus coronary artery disease risk.[13] [19,20,22]. Although there are different scoring systems available to ascertain the burden of coronary artery calcification and indirectly the coronary artery disease risk, visual coronary artery calcification score (V-CACS)[3,4] [21] can be easily adopted by reporting radiologists to be used in non-cardiac gated CT chest. There is no existing literature comparing V-CACS to both CT-SS and clinical severity in COVID-19. So the aim of this study is to ascertain the extent of coronary artery calcification, CT chest severity score, and their role in predicting clinical severity and outcome of COVID-19 patients.

2. Materials and methods

2.1. Patients and study group classification

The study was approved by institutional research board (IRB). We retrospectively studied patient's diagnosed with COVID-19 from March 1, 2020 to July 15, 2020 in our hospital. A total of 67 consecutive patients (64 male and 3 female) with COVID-19 confirmed by two times RT-PCR throat swab in whom an early disease non-cardiac gated CT Chest done within 1 to 9 days of symptom onset were included in the study.

Patients having other associated pre-existing chest abnormalities like sarcoidosis, interstitial lung disease, tuberculosis, bacterial pneumonia, primary or secondary malignancies affecting lung or pleura were excluded.

Clinically the patients were classified into mild, moderate, severe and critical categories. Mild cases are those who have mild clinical symptoms and may or may not require nasal oxygen. Moderate cases are those who have moderate clinical symptoms requiring nasal oxygen requirements. Severe cases are those who require ICU admission due to worsening clinical condition with the need for non-invasive ventilation and critical cases are the one that requires assisted invasive ventilation, ECMO etc.

Severe cases are the ones with atleast one of the following with clinical deterioration requiring ICU admission for non-invasive assisted ventilation like continuous oxygen or BIPAP;

1. Respiratory distress, RR $\geq$ 30/min
2. Resting oxygen saturation $<$ 93%
3. Partial pressure of the arterial blood oxygen PaO2 $\leq$ 300 mmHg

Critical cases are those meeting one of the following criteria;

1. Respiratory failure and the need for invasive mechanical ventilation or ECMO.
2. Requiring ICU admission due to organ failure.

For the study purpose we broadly had two groups, one group with the mild or moderate clinical symptoms falling into mild group while severe and critical groups were clubbed into a severe group. Primary outcome is defined as those patients having a clinically severe disease requiring ICU admission, assisted ventilation (like BIPAP, Ventilator or ECMO) or death. Based on the age of patients we divided the patient population into two groups, one group <50 years involving young and middle age and another group >50 years of age.

Past medical histories were obtained from hospital database or by self reporting by the patients including diabetes, hypertension, coronary heart disease, chronic kidney disease and body mass index (BMI), which were diagnosed according to standard criteria.

2.2. Image data collection

Image data was collected by 2 body imaging fellowship-trained radiologists with 9 and 14 years of experience (A.N. & D.K., respectively). Each of the radiologist scored every CT scans for V-CACS and CT-SS independent of each other. To minimize bias, reviewers were blinded to patient histories and clinical severity of COVID-19, other than COVID-19 positivity.

2.3. Visual coronary artery calcification score

The presence and severity of coronary artery calcification is visually assessed on soft tissue CT reconstruction, or if these are unavailable a CT lung construction is used. Coronary artery calcification is defined as an area of increased attenuation in the course of the coronary artery. Coronary artery calcification is assessed in each of the left mainstem, left anterior descending, left circumflex and right coronary artery branches. Coronary artery calcification in each vessel was visually assessed and assigned a score of 0 (none), 1 (mild), 2 (moderate) on 3 (severe) (Fig. 1). The V-CACS from each vessel will be summed to give a total coronary artery calcification score, which ranges from 0 to 12. This V-CACS was calculated based on 2016 Society of cardiovascular computed tomography (SCCT)/Society of thoracic radiology (STR) guidelines on coronary artery calcium scoring of non-cardiac chest CT scans.[3]

Fig. 2. 36 year old male from clinically mild group, having <50% involvement of left lower lobe- (apical subsegment) (a), posterior and lateral subsegments (b,c), giving a CT-SS left lobe SCORE-3; And <50% involvement of right lower lobe- (posterior and lateral subsegments-b,c), giving a CT-SS right lobe SCORE-2. The total CT-SS score is 3 +2 =5.

Fig. 3. 52 year old male from clinically severe group, (a-c) on right having >50% involvement of right upper lobe multiple subsegments; <50% involvement of middle lobe subsegments; >50% of all lower lobe subsegments. (a-c) On left <50% involvement of upper lobe subsegments; >50% involvement of lingula and left lower lobe subsegments. Total CT-SS is 30.

2.4. Chest CT severity score

Ran Yang et al., recently proposed a scoring system with a cut-off value based on CT chest assessment that correlates to clinical severity.[2] This pulmonary inflammation load score was seen to be higher in patients with clinically severe COVID-19 compared to patients with clinically mild disease. Mild cases require symptomatic treatment, while severe cases require ICU admission. The 18 subsegments of both lungs where divided into 20 regions, in which the left apico-posterior subsegment is divided into separate apical and posterior subsegmental regions and left antero-medial basal subsegment is divided into anterior and medial basal subsegments. CT-SS is defined by summing up individual scores from 20 lung subsegments visualized on CT chest scan, thereby giving a score to ascertain if the disease is severe or not. Score of 0, 1, 2 will be respectively assigned for each region if parenchymal opacification (like ground glassing, consolidation or air space infiltrates) involved 0%, <50%, >50% respectively of each region (Figs. 2, 3). The theoretical range of CT severity index ranges from 0 to 40. The optimal CT-SS threshold for severe COVID-19 is reported as 19.5 with 83.3% sensitivity and 94% specificity.[2]

2.5. Chest CT scan

Chest CT imaging was performed on a 640 detector CT scanner (Canon Acquilion one). All patients were examined in the supine position, with CT images acquired during end inspiration and hands raised by the side. The scanning range was from the apex of the lung to bilateral adrenals. CT scan parameters: X-ray tube parameter with automatic tube current modulation with kVp range 100–120, rotation time 0.5 s, pitch – high (PF-1.388/HP-111.0), section thickness 0.5 and 3 mm, collimation 0.5 × 80, intersection space 0.8 for the volume scan. Additional reconstruction with sharp convolution kernel and a slice thickness of 1.5 mm.

Table 1
Basic summary of included variables from 67 COVID-19 patients.

Variables	Median	Min- Max
Age (years)	45	24–75
Right lobe CT-SS	12.5	0–20
Left lobe CT-SS	11	0–20
CT-SS	23.5	0–40
CACS	3.5	0–10.5
Variables	**Frequency**	**Percentage**
Gender		
Male	64	95.5%
Female	3	4.4%
ICU		
Yes	23	34.3%
No	44	65.7%
Oxygen		
Yes	40	59.7%
No	27	40.3%
BIPAP		
Yes	14	20.9%
No	53	79.1%
Ventilated		
Yes	14	20.9%
No	53	79.1%
ECMO		
Yes	2	3%
No	65	97%
Outcome		
Discharge	64	95.5%
Death	3	4.5%

2.6. Statistical analysis

The statistical analysis was performed using SPSS (IBM, Armonk, New York, USA) and MedCalc software (MedCalc Software Ltd., Belgium). Data were checked for normality distribution using the

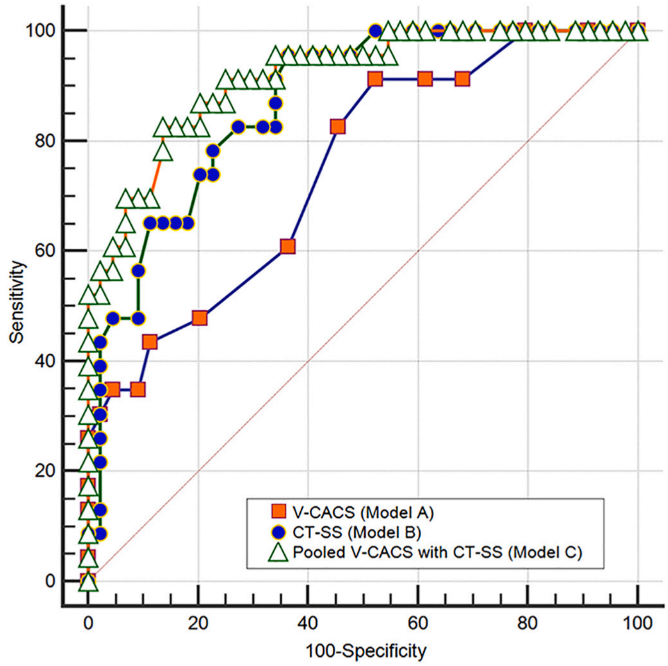

Fig. 4. Receiver operating characteristic (ROC) curves of three models; V-CACS (Model-A), CT-SS (Model-B), and Pooled V-CACS with CT-SS (Model-C) for differentiation of clinically mild and clinically severe disease group.

Shapiro-Wilk test. Quantitative data is expressed as median and interquartile range and qualitative data is presented with numbers (percentage). Inter-ratter reliability is evaluated using the Kappa coefficient for categorical variables and Intraclass correlation coefficient for continues variables, between the two observers. Mann-Whitney test and Chi-squares or Fisher's exact test were used for group comparison. Logistic regression analyses was performed with the dependent variable, in need for external support (oxygen, BIPAP, ventilation, ECMO and ICU) and independent variables including sex, age, CT scores (CTSS and V-CACS), Diabetes mellitus, Hypertension, Coronary artery disease (CAD), Chronic kidney disease (CKD), Body Mass Index (BMI) to identify independent predictors of assisted ventilation in patients admitted in ICU and death. ROC curves analysis is performed for the assessment of performance. Pearson correlation coefficients were used to assess the presence of associations between CT score and age of patient population.

3. Results

A total of 67 COVID-19 positive patients were included (median age of 45 years, age range of 24 to 75; with 64 males and 3 females). 64 cases were discharged and 3 patients died during their course of stay in hospital (Table 1). The median CT-SS was 23.5 (ranged from 0 to 40), median V-CACS was 3.5 (ranged from 0 to 10.5). All discharged patients were followed up for 1 month from the date of inpatient discharge. 24 patients (35.8%) had one or more past disease co morbidities, of which hypertension was the most common in 16 cases (23.8%).

Two radiologists independently scored V-CACS and CT-SS and observed excellent agreement. Inter-rater reliability and the Intraclass correlation coefficients were 0.95 (95%; CI 0.91 to 0.97) for V-CACS and 0.98 (95% CI: 0.97 to 0.99) for CT-SS.

In receiver operating characteristic (ROC) curve analysis, V-CACS with cut off value of 3 had clinically severe disease, requiring ICU admission and assisted ventilation (82.67% sensitivity, 54.55% specificity, PPV 48.7%, NPV 85.7%, AUC 0.75; 95% CI: 63%- 85%; Fig. 4, Model A). CT-SS, with a cut of value of 21.5 had clinical severe disease, requiring ICU admission and assisted ventilation (95.7% sensitivity, 63.6% specificity, PPV 57.9%, NPV 96.6%, AUC of 0.87; 95% CI: 77%- 94%; Fig. 4, Model B). When pooling the V-CACS with CT-SS the area under the curve was 0.92 (82.6% sensitivity, 86.4% specificity, PPV 76%, NPV 90.5%, 95% CI: 82%- 97%; Fig. 4, Model C).

On regression analysis (Table 2), V-CACS and CT-SS are individual independent predictors of COVID-19 severity (Odds ratio, 1.72; 95% CI, 0.99–2.98; $p = 0.05$ and Odds ratio, 1.22; 95% CI, 1.08–1.39; $p = 0.001$; respectively). The area under the curve (AUC) for combined V-CACS and CT-SS (model C) was 0.96 (95% CI 0.84–0.98), with correctly predicted 82.1% cases.

We observed significant positive correlation of V-CACS with age ($r = 0.41$; p = 0.001) (Fig. 5a) and trend level positive correlation of CT-SS with age ($r = 0.22$; $p = 0.08$) (Fig. 5b), and significant positive correlation between V-CACS and CTSS ($r = 0.27$; $p = 0.026$) (Fig. 5c). The presence of co-morbidities such as hypertension, diabetes, CAD, CKD or BMI did not reach the level of statistical significance, to be called as independent predictors of COVID-19 clinical severity, ICU admission, assisted ventilation or death. (Table 2).

3.1. *Secondary outcome data between comparison groups*

On comparison between clinically mild and severe group (Table 3), the median age of mild group was 39.5 (interquartile range of 24–75) while in severe group the median age was 57 (interquartile range of 31–71), $p = 0.002$. The median V-CACS in mild group was 3, and 4 in severe group, $p = 0.001$ (Fig. 6D). The median CT-SS in mild group was 20, and 32.5 in sever group, p = 0.001 (Fig. 6A). Between the mild and severe group, there was statistical significance on the need for oxygen, BIPAP, ventilation and ICU in severe cases, $p = 0.001$. In mild group there was no death, while in severe group there was 3 deaths, $p = 0.03$.

On comparison between mild CT-SS (CT-SS <21.5) and severe CT-SS group (CT-SS >21.5) (Table 3), the median age was 39 (interquartile range of 24–75) while in severe group the median age was 50.5 (interquartile range of 31–71), $p = 0.07$. The median V-CACS in mild group was 3.5, and 3.5 in severe group, $p = 0.34$ (Fig. 6B). The median CT-SS in mild group was 17, and 32 in sever group, $p = 0.001$ (Fig. 6E; the bar figures). Between the mild and severe CT-SS group, there was statistical significance on the clinical severity and the need for oxygen, BIPAP, ventilation and ICU in severe group, $p < 0.05$. There was no statistical significance between the two groups on outcome like discharge or death.

Table 2
Regression analysis table showing factors tested for association with COVID-19.

Variables	Coefficient (B)	SE	Wald value	*P* value	Odd ratio Exp(B)	95% CI	
Age	0.01	0.04	0.01	0.97	1.00	0.911	1.10
Sex	−12.8	1.90E4	0.00	0.99	0.00	0.000	–
V-CACS	0.54	0.27	3.8	0.05	1.72	0.99	2.98
CT-SS	0.20	0.63	10.55	0.001	1.22	1.08	1.39
Hypertension	−1.59	1.33	1.43	0.23	0.20	0.015	2.75
Diabetes	2.44	1.37	3.19	0.07	11.5	0.788	169.7
CAD	1.86	1.79	1.07	0.30	6.42	0.190	217.3
CKD	27.22	2.76E4	0.00	0.99	6.66E11	0.000	–
BMI	0.027	0.103	0.07	0.79	1.02	0.841	1.256
Constant	−9.157	3.606	6.44	0.01	0.000		

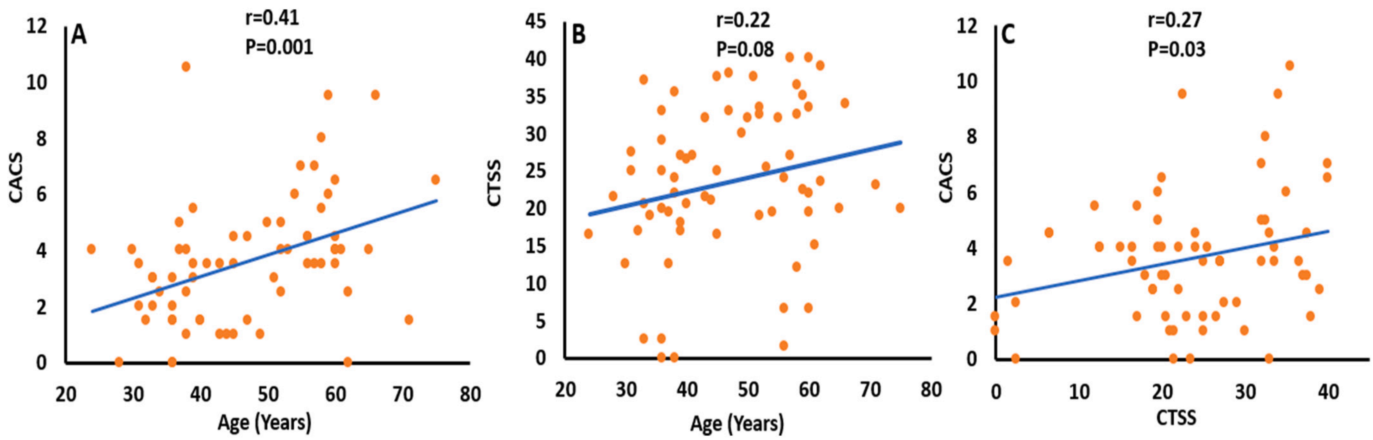

Fig. 5. Showing correlation of V-CACS, CT-SS with age. (a) Significant positive correlation of V-CACS with age ($p = 0.001$); (b) Insignificant positive correlation of CT-SS with age ($p = 0.08$); (c) Significant positive correlation of CT-SS with V-CACS ($p = 0.03$).

On comparison between less than 50 years and more than 50 years group (Table 3). The median V-CACS in age <50 group was 2.5, and 4.3 in >50 years age group, $p = 0.001$ (Fig. 6C; the bar figures). The median CTSS in age <50 group was 21.5, and 24.8 in >50 years age group, $p = 0.15$ (Fig. 6F). Between two group, there was statistical significance on the clinical severity and the need for oxygen, BIPAP, ventilation and ICU admission in group >50 years, $p < 0.05$. There was no statistical significance between the age groups on outcome like discharge or death.

4. Discussion

This study evaluated the ability of V-CACS in predicting clinically severity and outcome in COVID-19, using semi-quantitative scoring of coronary artery calcifications. In our study, we found that the presence of coronary artery calcifications with a visual score of 3 and above is an independent predictor of clinical severity, including the requirement of an ICU admission, assisted ventilation or death in hospitalized patients. Models combining V-CACS and CT-SS, where highly accurate in predicting the clinical severity and outcome, than CT-SS and V-CACS independently. Our results indicate patients with a known COVID-19, in whom there is an inpatient CT scan the V-CACS and CT-SS above the threshold will help to identify potential clinically severe disease.

Dillinger JG et al. was the first to evaluate the utility of coronary artery calcifications in relation to primary outcome in patients with COVID-19 using the Agatston scoring on non-cardiac gated CT chest, demonstrating that presence and severity of coronary artery calcification is associated with a worse prognosis in patients with COVID-19.[23] The severity of immune response, endothelial dysfunction and myocardial stress due to COVID-19 was hypothesized to be exacerbated in patients with subclinical coronary atherosclerosis.[23] In our study, we found that the V-CACS score was higher in clinically severe disease compared to clinically mild disease and there was increased requirement for oxygen support, need for ICU admission, assisted ventilation or deaths in patients with high V-CACS. We also observed significant positive correlation of V-CACS with age suggesting that age has significant impact in the prognostication of COVID-19 patients.

The CT-SS proposed by Ran Yang et al., used a semi-quantitative scoring method using the extend of lung opacification involving 20 lung regions, demonstrated that CT-SS was higher in clinically severe disease compared to clinically mild cases.[2] They determined that the threshold of 19.5 could identify severe COVID-19, with a sensitivity of 83.3% and specificity of 94%, resulting in NPV of 96.3%. In our study, adopting the same lung scoring system, we found that a CT-SS cut off value of 21.5 is an independent predictor of clinical severity, with CT-SS more than 21.5 requiring ICU admission or assisted ventilation during the clinical course of the disease.

This retrospective study has several limitations. First, majority of patients admitted in our hospital were male patient's as there was dedicated female COVID-19 in-patient admission arranged elsewhere. Second, validation studies conducted in multiple centers with higher sample size are still necessary to determine the validity of V-CACS. Third, there could have been clinically severe disease in whom there was a worse outcome of death, that could not be included in this study due to lack of a CT scan being taken during the hospital stay. Fourth, Although several authors have observed the presence of co-morbidities as individual independent predictors of COVID-19 severity and outcome, in our study however we did not observe any significant effect of co-morbidities as independent predictors of clinical severity and outcome, may be due to small sample size or less severe status of co-morbidities.

In conclusion, our study demonstrates that independently and in-combination use of semi-quantitative V-CACS and CT-SS assessment, was highly accurate in predicting clinically severe cases of COVID-19, including the requirement for ICU admission or assisted ventilation. Our results may enable the radiologists in including both V-CACS and CT-SS in their reporting format, that will help clinicians in triaging the patients appropriately in their clinical practice and possibly avert a worse potential outcome in COVID-19.

Author contributions section

Guarantor of integrity of entire study A.N. Study concepts/ study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, P.N, M.H, D.K, A. N.; clinical studies, D.K, A.N.; Data manager/collection: B.J.; Methodology, statistical analysis, S.K.Y, A.N; and manuscript editing, S.K.Y, B.J, M.H, D.K, A.N.

Declaration of competing interest

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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Table 3
Comparison of different groups classified on basis of clinical symptoms, CT-SS and age groups.

Parameters	Clinically mild ($n = 44$)	Clinically severe ($n = 23$)	U value	p value
Age				
Median	39.5	57	271	0.002
Min-Max	24–75	31–71		
Gender				
Male	42(95.5%)	22 (95.7%)	–	1.0
Female	2 (4.5%)	1 (4.3%)		
Outcome				
Discharge	44 (100%)	20 (87%)	–	0.03
Death	0 (0%)	3 (13%)		
Oxygen				
Yes	17 (39%)	23 (100%)	–	0.001
No	27 (61%)	0(0%)		
BIPAP				
Yes	0 (0%)	14(60.9%)	–	0.001
No	44 (100%)	9 (39.1%)		
Ventilated				
Yes	0 (0%)	14 (60.9%)	–	0.001
No	44 (100%)	9 (39.1%)		
ICU				
Yes	0 (0%)	23 (100%)	–	0.001
No	44 (100%)	0 (0%)		
ECMO				
Yes	0 (0%)	2 (8.7%)	–	0.11
No	44 (100%)	21 (91.3%)		

Parameters	Mild CT-SS ($n = 29$)	Severe CT-SS ($n = 38$)	U value	p value
Age				
Median	39	50.5	406	0.07
Min-max	24–75	31–71		
Gender				
Male	27(93%)	37 (97%)	–	0.6
Female	2 (7%)	1 (3%)		
Outcome				
Discharge	29 (100%)	35 (92%)	–	0.25
Death	0 (0%)	3 (7%)		
Oxygen				
Yes	8 (28%)	32(84%)	–	0.001
No	21 (72%)	6 (16%)		
BIPAP				
Yes	0(0%)	14 (37%)	–	0.001
No	29 (100%)	24 (63%)		
Ventilated				
Yes	1(3%)	13 (34%)	–	0.002
No	28 (97%)	25 (65%)		
ICU				
Yes	1(3%)	22(58%)	–	0.001
No	28 (97%)	16 (42%)		
ECMO				
Yes	0(0%)	2 (5.3%)	–	0.5
No	44 (100%)	36 (94.7%)		

Parameters	Age < 50 ($n = 37$)	Age > 50 ($n = 30$)	U value	p value
Age	’			
Median	38	58	0.00	0.001
Min-max	24–49	50–75		
Gender				
Male	34 (91.9%)	30 (100%)	–	0.25
Female	3 (8.1%)	0 (0%)		
Outcome				
Discharge	37 (100%)	27 (90%)	–	0.54
Death	0 (0%)	3 (10%)		
Oxygen				
Yes	17(46%)	23(77%)	–	0.01
No	20 (54%)	7 (23%)		
BIPAP				
Yes	3 (8%)	11 (37%)	–	0.006
No	34 (92%)	19 (63%)		
Ventilated				
Yes	4 (11%)	10 (33%)	–	0.04

(*continued on next page*)

Table 3 (*continued*)

Parameters	Age < 50 (*n* = 37)	Age > 50 (*n* = 30)	U value	p value
No	33 (89%)	20 (67%)		
ICU				
Yes	6 (16%)	13(43%)	–	0.001
No	31 (84%)	17 (57%)		
ECMO				
Yes	1(3%)	1(3%)	–	1
No	36 (97%)	29 (97%)		

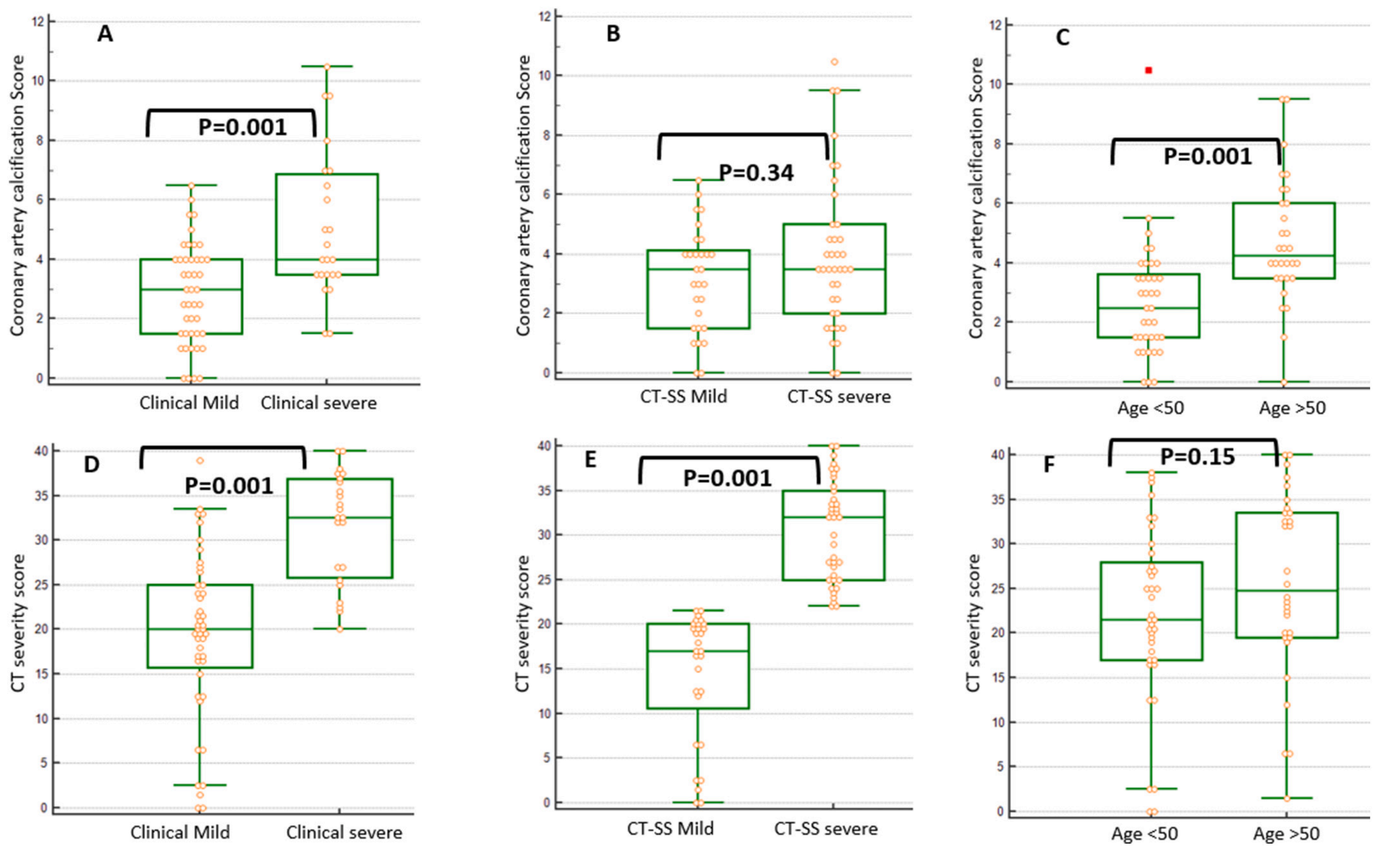

Fig. 6. Comparison of V-CACS with different groups; (A) Significantly higher V-CACS score in clinically severe group compared to clinically mild, p = 0.001; (B) Insignificant V-CACS score in CT-SS severe group compared to CT-SS mild, *p* = 0.34; (C) Significantly higher V-CACS score in age group more than 50 years compared to age group less than 50 years, *p* = 0.001. Comparison of CT-SS with different groups; (D) Significantly higher CT-SS score in clinically severe group compared to clinically mild, p = 0.001; (E) Significantly higher CT-SS score in CT-SS severe group compared to CT-SS mild, p = 0.001; (F) Insignificant CT-SS score in age group more than 50 years compared to age group less than 50 years, *p* = 0.15.

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