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Predicting the 30-day Adverse Outcomes of Non-Critical New-Onset COVID-19 Patients in Emergency Departments based on their Lung CT Scan Findings; A Pilot Study for Derivation an Emergency Scoring Tool

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Abstract

Introduction: Coronavirus Disease (COVID-19) has become the most important global health issue, and chest computed tomography (CT) scan can help determine the severity of the infection.

Objectives: This study aimed to provide an emergency scoring tool for predicting 30-day adverse outcomes in non-critical new-onset COVID-19 patients.

Methods: This derivation study was conducted on new-onset COVID-19 patients presenting to the emergency department of an urban teaching hospital in Tehran, Iran, between 20 February and 20 March 2020. The total lobe severity score (TSS), age, history of comorbidities, and 30-day adverse outcomes (death, ICU admission or intubation) were taken into account to produce three prediction models.

Results: Overall, 137 patients were included in the study. Their mean age was 59.9±16.8 years and 62% were male. The ground glass nodule, patch B/punctate ground-glass opacity, fibrous stripes, and air bronchogram sign with perihilar distribution, bilateral and ≥ 2 affected lobes were the most common findings. The mean TSS (model 1) was significantly higher in patients with an adverse outcome (9.4±3.2) compared to the discharged patients (7.2±3.3) (p<0.001, AUC: 0.703, sensitivity: 64.4% and specificity: 74.1%). The optimal cut-off point of model 2 (TSS and age) had the following parameters: AUC: 0.721, sensitivity: 71.2% and specificity: 67.2%. The optimal cut-off point of model 3 (TSS, age, comorbidities) had: AUC: 0.755, sensitivity: 79.7% and specificity: 65.5%. The discrimination achieved with model 3 based on Bonferroni's test was significantly better than that achieved with TSS (p<0.001).

Conclusion: TSS combined with age and history of at least one comorbidity had a better predictive value for adverse outcomes with a cut-off point above 8.

Key words: COVID-19; Patient Outcome Assessment; Prognosis; Scoring System; X-Ray Computed Tomography

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Introduction

COVID-19 is a highly contagious disease that is spreading worldwide at an alarming rate. Currently, the pandemic is of paramount importance and poses a serious threat to public health and requires global collaboration to be controlled (1). In most cases, COVID-19 presents with unspecific symptoms such as dry cough, fever, and fatigue, but it is a life-threatening disease that can cause serious medical conditions (2-5). The clinical course of COVID-19 infection differs from one patient to another and varies from no symptoms to respiratory failure, septic shock, and coagulation dysfunction (6-10).

Several studies have recommended chest computed tomography (CT) scan as a diagnostic and also prognostic tool in COVID-19 patients (11-15). A cohort study among 1014 patients in Wuhan, China, reported that chest CT scan had 97% sensitivity, 25% specificity, and 68% accuracy in the diagnosis of COVID-19 (16). Based on the existing studies, peripheral ground-glass opacity is the most frequent and typical finding of COVID-19 infection in chest CT scans (17, 18). Other findings, such as consolidations, vascular changes, bronchial wall thickness, pleural effusion, the crazy-paving sign, halo and reversed-halo sign, reticular pattern, and fibrotic pattern are mostly observed in the recovery phase of the disease (19-21).

Like other diseases, the prognosis of COVID-19 patients is of undisputed importance and requires clinical and paraclinical details. Several studies have shown that there is a correlation between chest CT scan findings and prognosis of the patients. For example, One study revealed that CT scan findings in patients with severe lung involvements have mostly had central patterns (22). Some studies found that a poor prognosis of COVID-19 was mostly related to higher chest involvements on the CT scan (23, 24). The development of pulmonary consolidation may be a red flag of severe disease (25). Likewise, several studies have reported that patients with severe COVID-19 infection have shown a higher rate of bronchial wall thickness, the crazy-paving sign, mediastinal lymphadenopathy, and pleural effusion in their chest CT scans (13, 26, 27).

There is no rapid scoring tool based on qualitative and quantitative findings that can help predict the patient outcomes upon their emergency department (ED) admission. The aim of this study was to provide a prognostic assessment tool based on chest CT scan findings to predict 30-day adverse outcomes in new-onset COVID-19 patients who were hemodynamically stable and did not require immediate critical care at the time of ED admission.

Methods

Study design

This derivation study was conducted at the ED of a university-affiliated hospital in Tehran, Iran. The implementation of the project was approved by the ethics committee of Tehran University of Medical Sciences. All the data obtained were analyzed and reported anonymously.

Study population

All people over 18 years of age with new-onset COVID-19 symptoms (over the past 72 hours) presenting to the ED from 20 February to 20 March, 2020, were included. Convenience sampling was used in this research. As this was a pilot study, we applied the rule of thumb to estimate the sample size.

The primary diagnosis of COVID-19 was made based on a physical examination and paraclinical tests. The patients underwent a chest CT scan immediately after their ED admission. Siemens® Somatom Emotion multi-slice CT scanner was used for this purpose, as it allows high-resolution thin slice scanning with collimation as thin as 16*0.6 mm or 6*0.5 mm.

In addition, the reverse transcription-polymerase chain reaction (RT-PCR) test was performed in all the patients as the gold standard test. Two nasopharyngeal specimens were obtained immediately after the admission and the following day in this regard.

The exclusion criteria were as follows: Having unstable clinical conditions (loss of consciousness, unstable hemodynamic status, shock index more than one, and respiratory failure requiring immediate invasive mechanical ventilation), needing immediate critical care at the time of ED admission, pregnancy (as these candidates were referred to the nearest women's hospital), those leaving the ED against medical advice or having had two consecutive negative RT-PCR test results.

Data collection

Demographic data, including age, gender, and comorbidities, including hypertension (HTN), diabetes mellitus (DM), chronic renal failure (CRF), coronary artery disease (CAD), and cirrhosis, were extracted from the medical documents of the patients. A radiologist reported the findings, including the number of affected lobes, appearance of ground-glass nodules, patch B/punctate ground-glass opacities, patch C consolidations, fibrous stripes, irregular solid nodules, cavitation, pleural effusion, pleural thickness, signs of pleural reaction, lymphadenopathy, calcification, bronchiectasis, the reversed-halo sign, the crazy-paving sign, bronchial wall thickness, pulmonary emphysema, air bronchogram signs and vascular enlargement, lobe severity score, lateralization of findings, i.e., bilateral or unilateral, distribution of findings, i.e., subpleural, perihilar, central, focal, multifocal, and diffused.

The severity of lung involvement was evaluated in the five lung lobes and scores of 0, 1, 2, 3, and 4 were taken as none (0%), minimal (1 to 25%), mild (26 to 50%), moderate (51 to 75%), and severe (76 to 100%) lung involvement, respectively (28). The total lobe severity score (TSS) was calculated by summing up the scores from the five lobes (left upper lobe, left lower lobe, right upper lobe, right middle lobe, and right lower lobe).

Finally, the patient outcomes (after 30 days), including death, ICU admission with or without intubation, or discharge from the hospital, were extracted from their medical documents. The outcome was also divided into two different groups, including adverse outcomes (death or ICU admission with or without intubation) and discharge from the hospital.

Eventually, TSS was used as a prediction tool based on the chest CT scan findings for the adverse outcomes of COVID-19. We categorized age into above and under 60 years old and added one score to TSS for patients over age 60 years, and named it model 2. In addition, in model 3, we added one score to model 2 for patients with at least one comorbidity such as HTN, DM, CRF, and CAD. Finally, the accuracy of these three models in predicting adverse outcomes was examined.

Statistical analysis

All the statistical analyses were performed using STATA 14 (StataCorp, Texas, USA). The Kolmogorov-Smirnov test was used to assess the normal distribution of the variables. Continuous variables were described using the mean ± SD, and categorical variables using frequency and percentage of the data. Due to the normality of the variables' distribution, parametric tests were applied to investigate the relationship between the variables. The relationship between the continuous and categorical variables was examined using the Independent-Sample t-test and the one-way ANOVA.

The relationship between the categorical variables was examined using the Chi-square test or Fisher's Exact test. The sensitivity, specificity, positive likelihood ratio (PLR), and negative likelihood ratio (NLR) of different cut-off points of the TSS, model 2 (TSS with age) and model 3 (model 2 with comorbidity) scores were calculated and presented with a 95% confidence interval (CI). The ROC curve and the area under the curve (AUC) were also examined, and the AUC difference of model 2 and 3 with TSS compared with the Chi-square test and Bonferroni's method. The optimal cut-off point was determined based-on Youden's J statistic. $P < 0.05$ was considered statistically significant.

RESULTS

In our study, 187 patients were recruited, of whom 50 patients left the ED against medical advice, and 137 patients with a mean age of 59.9±16.8 years (62.0% male) were included in the final analysis. The frequency of death, ICU admission with or without intubation, and discharged patients was 49 (35.8%), 22 (16.1%), and 66 (48.2%), respectively. The mean age in patients with adverse outcomes was 66.6±14.6, which is significantly higher than the mean age of the discharged patients (59.2±16.2) (p<0.001). Also, the history of HTN, DM, CRF, or CAD was significantly higher in patients with adverse outcomes than the discharged patients. The history of HTN, DM, CRF, and CAD was significantly higher in those with adverse outcomes (78.9%) than the discharged patients (24.2%) (p<0.001) (Table 1).

Of the 137 patients who underwent chest computed tomography, the prevalence of patients with 0, 1, and ≥ 2 affected lobes was 4.5%, 13.6%, and 81.9%, respectively. The adverse outcome was significantly higher in patients with more than two lung-affected lobes (93.0% vs. 81.8%, p=0.048). The prevalence of bilateral lung involvement was 94.8%. The most common chest CT scan findings were patch B/punctate ground-glass opacity (92.0%), ground glass nodule (67.2%), air bronchogram signs (61.3%) and fibrous stripes (58.4%).

Of the CT scan findings, patch B/ punctate ground-glass opacity (97.2% vs. 86.4%, p=0.020), bronchiectasis (29.6% vs. 10.6%, p=0.006), the crazy-paving sign (29.6% vs. 4.5%, p<0.001) was significantly higher in patients with adverse outcomes than the discharged patients. Nevertheless, lymphadenopathy was significantly higher in the discharged patients (4.2% vs. 19.7%, p=0.005).

Table 1: The distribution and relationship between demographic variable and comorbidities and the patient's outcome

	Total (n=137)	Adverse Outcome		Discharge (n=66)	P-Value [a]	P-Value [b]
		Death (n=49)	ICU and/or Intubation (n=22)			
Age, mean±SD	59.9±16.8	70.1±12.8	58.7±15.5	52.9±16.2	<0.001	<0.001
Sex; male, n (%)	85 (62.0)	29 (59.2)	14 (63.6)	42 (63.6)	0.876	0.711
Comorbidities, n (%)						
Hypertension	46 (33.6)	26 (53.1)	7 (31.8)	13 (19.7)	0.001	0.001
Diabetes Mellitus	29 (21.2)	21 (42.9)	6 (27.3)	2 (3.0)	<0.001	<0.001
Chronic Renal Failure	11 (8.0)	8 (16.3)	3 (13.6)	0 (0.0)	0.001	0.001
Coronary Artery Disease	50 (36.5)	29 (59.2)	11 (50.0)	10 (15.2)	<0.001	<0.001
Cirrhosis	3 (2.2)	2 (4.1)	0 (0.0)	1 (1.5)	0.749	1.0

ICU: Intensive Care Unit; SD: Standard Deviation.

[a]P-value refers to the relationship of each variable between three patients' outcomes;

[b]P-value refers to the relationship of each variable between two patients' outcome (adverse outcomes and discharge)

The perihilar (p=0.014), central (p<0.001), and diffused (p<0.001) distribution of CT scan findings was significantly higher in patients with adverse outcomes, but multifocal distribution was significantly higher in the discharged patients (p<0.001) (Table 2). The prevalence of cavitation and vascular enlargement was zero.

The mean severity lobe score in all five lobes was significantly higher in the patients with adverse outcomes. The mean TSS in patients with adverse outcomes (9.4 ±3.2) was significantly higher than in the discharged patients (7.2±3.3) (p<0.001).

The ROC analysis showed that the AUC of TSS for the prognosis of adverse outcomes was 0.703 (95% CI: 0.607 to 0.799). The optimal cut-off point of TSS had sensitivity and specificity in this cut-off point and was 64.4% and 74.1%, respectively.

In the second predicting model (TSS with age), the AUC was 0.721 (95% CI: 0.628 to 0.814) and the sensitivity and specificity in the optimal cut-off point were 71.2% and 67.2%, respectively.

In the third predicting model (TSS with age and comorbidity), the AUC was 0.755 (95% CI: 0.666 to 0.844), and the optimal cut-off point had 79.7% sensitivity and 65.5% specificity. The optimal cut-off point was more than 8 in all the three models (Table 3). The discrimination of model 3 based on Bonferroni's test was significantly better than TSS (p<0.001), but model 2 was not significantly different with TSS (p=0.071) (Figure 1).

Table 2: The distribution and relationship between the chest CT scan findings and the patient outcomes

	Total (n=137)	Adverse Outcome		Discharge (n=66)	P-Value [a]	P-Value [b]
		Death (n=49)	ICU and/or Intubation (n=22)			
Severity lobe score, mean±SD						
LUL	1.2±0.73	1.4±0.79	1.4±0.82	0.93±0.57	0.002	<0.001
LLL	1.9±1.1	2.2±0.94	2.1±1.2	1.7±1.0	0.014	0.004
RUL	1.1±0.71	1.4±0.66	1.2±0.83	0.97±0.64	0.008	0.004
RML	1.9±0.86	2.2±0.79	1.8±0.83	1.7±0.87	0.005	0.013
RLL	2.0±1.1	2.4±0.99	1.8±0.98	1.8±1.1	0.008	0.030
TSS	8.3±3.4	9.8±2.9	8.4±3.5	7.2±3.3	0.001	<0.001
More than two lobes affected, n (%)	120 (87.6)	46 (93.9)	20 (90.9)	54 (81.8)	0.133	0.048
CT scan findings*, n (%)						
Ground glass nodule	92 (67.2)	35 (71.4)	16 (72.7)	41 (62.1)	0.479	0.227
Patch B/punctate ground-glass opacity	126 (92.0)	47 (95.9)	22 (100)	57 (86.4)	0.073	0.020
Patch C consolidation	63 (46.0)	27 (55.1)	7 (31.8)	29 (43.9)	0.171	0.643
Fibrous stripes	80 (58.4)	34 (69.4)	10 (45.5)	36 (54.5)	0.113	0.378
Irregular solid nodule	55 (40.1)	24 (49.0)	7 (31.8)	24 (36.4)	0.270	0.384
Pleural effusion	7 (5.1)	5 (10.2)	0 (0.0)	2 (3.0)	0.191	0.443
Pleural thickness	56 (40.9)	29 (59.2)	3 (13.6)	24 (36.4)	0.001	0.300
Pleural reaction signs	29 (21.2)	13 (26.5)	0 (0.0)	16 (24.2)	0.028	0.396
Lymphadenopathy	16 (11.7)	3 (6.1)	0 (0.0)	13 (19.7)	0.014	0.005
Calcification	4 (2.9)	1 (2.0)	0 (0.0)	3 (4.5)	0.656	0.352
Bronchiectasis	28 (20.4)	18 (36.7)	3 (13.6)	7 (10.6)	0.002	0.006
Reversed halo sign	13 (9.5)	2 (4.1)	2 (9.1)	9 (13.6)	0.220	0.110
The crazy-paving sign	24 (17.5)	15 (30.6)	6 (27.3)	3 (4.5)	0.001	<0.001
Bronchial wall thickness	51 (37.2)	23 (46.9)	4 (18.2)	24 (36.4)	0.067	0.840
Pulmonary emphysema	3 (2.2)	1 (2.0)	0 (0.0)	2 (3.0)	1.0	0.609
Air bronchogram signs	84 (61.3)	33 (67.3)	12 (54.5)	39 (59.1)	0.518	0.606
Distribution, n (%)						
Subpleural	120 (87.6)	46 (93.9)	16 (72.7)	58 (87.9)	0.044	0.922
Perihilar	128 (93.4)	48 (98.0)	22 (100)	58 (87.9)	0.062	0.014
Central	53 (38.7)	32 (65.3)	11 (50.0)	10 (15.2)	<0.001	<0.001
Focal	7 (5.1)	3 (6.1)	1 (4.5)	3 (4.5)	0.879	1.0
Multifocal	51 (37.2)	12 (24.5)	2 (9.1)	37 (56.1)	<0.001	<0.001
Diffused	31 (22.6)	20 (40.8)	8 (36.4)	3 (4.5)	<0.001	<0.001
Bilateral lungs, n (%)	127 (94.8)	48 (98.0)	21 (95.5)	58 (92.1)	0.334	0.253

SD: Standard Deviation; ICU: Intensive Care Unit; LUL: Left Upper Lobe; LLL: Left Lower Lobe; RUL: Right Upper Lobe; RML: Right Middle Lobe; RLL: Right Lower Lobe; TSS: Total Lobe Severity Score; CT: Computed Tomography.

[a]P-value refers to the relationship of each variable between three patients' outcomes;

[b]P-value refers to the relationship of each variable between two patients' outcomes (Adverse outcomes and discharge)

Table 3: The accuracy indices of TSS, model 2 (TSS with age) and model 3 (model 2 with comorbidity) for adverse outcomes of COVID-19

Cut-Off Point	Model	Sensitivity	Specificity	PLR	NLR
		(95% CI)			
>7	TSS	76.27 (63.4 - 86.4)	55.17 (41.5 - 68.3)	1.70 (1.2 - 2.3)	0.43 (0.3 - 0.7)
	Model-2	81.36 (69.1 - 90.3)	50.00 (36.6 - 63.4)	1.63 (1.2 - 2.2)	0.37 (0.2 - 0.7)
	Model-3	86.44 (75.0 - 94.0)	46.55 (33.3 - 60.1)	1.62 (1.2 - 2.1)	0.29 (0.1 - 0.6)
>8*	TSS	64.41 (50.9 - 76.4)	74.14 (61.0 - 84.7)	2.49 (1.5 - 4.0)	0.48 (0.3 - 0.7)
	Model-2	71.19 (57.9 - 82.2)	67.24 (53.7 - 79.0)	2.17 (1.5 - 3.3)	0.43 (0.3 - 0.7)
	Model-3	79.66 (67.2 - 89.0)	65.52 (51.9 - 77.5)	2.31 (1.6 - 3.4)	0.31 (0.2 - 0.5)
>9	TSS	47.46 (34.3 - 60.9)	82.76 (70.6 - 91.4)	2.75 (1.5 - 5.1)	0.63 (0.5 - 0.8)
	Model-2	57.63 (44.1 - 70.4)	75.86 (62.8 - 86.1)	2.39 (1.4 - 4.0)	0.56 (0.4 - 0.8)
	Model-3	67.80 (54.4 - 79.4)	72.41 (59.1 - 83.3)	2.46 (1.6 - 3.9)	0.44 0.3 - 0.7)

CI: Confidence Interval; PLR: Positive Likelihood Ratio; NLR: Negative Likelihood Ratio; TSS: Total Lobe Severity Score. Model 2: TSS with age; Model 3: Model 2 with comorbidity.

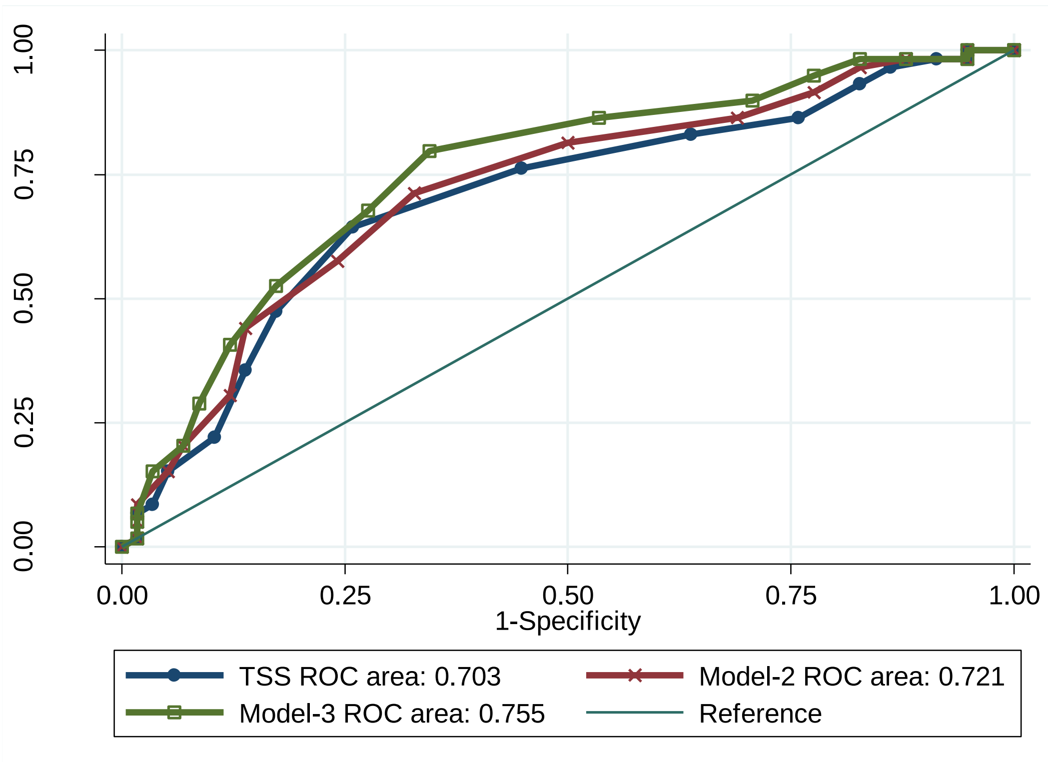

Figure 1: The area under the ROC curve for TSS, model 2 (TSS with age) and model 3 (model 2 with comorbidity) for adverse outcomes of COVID-19

Discussion

In the present study, the chest CT scan findings and demographic data of non-critical new-onset COVID-19 patients were evaluated to develop a useful tool for predicting the patients' adverse outcomes. TSS, model 2 and model 3 were developed based on the chest CT scan findings, age range, and presence of at least one comorbidity. The results showed that TSS was significantly higher in those with adverse outcomes, and model 3 at the cut-off point of more than 8 provided an acceptable sensitivity, specificity, and AUC for predicting adverse outcomes. The discrimination of model 3 was significantly better compared to TSS, but model 2 did not differ significantly with TSS.

Previous studies have shown that some chest CT scan findings are more common in patients with severe COVID-19 infection. Khunhua et al. compared 25 critical cases of COVID-19 with 58 controls and found that the frequency of consolidation, linear opacity, the crazy-paving sign, and bronchial wall thickness and TSS were higher in the critical cases (29). This result was consistent with the present findings, but our different frequent CT scan findings may be attributed to the assessment of critical cases in Khunhua's research and non-critical cases in our study.

Our study showed that CT-scan findings were mostly distributed peripherally and bilaterally. Similarly, Zhao et al. conducted a study on the chest CT scan findings of 101 COVID-19 patients and showed that 87.1% and 82.2% of the patients had peripheral distributions and bilateral involvements (27). The most common lesions in the CT scan findings in our study were ground-glass opacity, followed by ground glass nodules. These results are consistent with the findings of some other studies (17-19). Contrary to our findings, one study revealed that the frequency of pleural effusion was higher in the patients with severe COVID-19 infection, which may reflect their higher viral load (27). Our study found no significant relationship between pleural effusion and the patients' outcomes.

Many reports have assessed chest CT scan findings in COVID-19 patients (18, 30) as well as their clinical features (31, 32), but providing a rapid scoring tool for use in the ED is a notable achievement of this study. In this research, model 3, which consists of TSS, age, and history of at least one comorbidity, was used to predict the probability of 30-day adverse outcomes. This prediction model can be applied to quickly detect the probability of death and ICU admission in COVID-19 patients who are initially stable at the time of ED admission. Therefore, this model can prompt medical teams to pursue more proficient monitoring and patient care to avoid adverse outcomes.

Limitations

An important drawback of the present study was its small sample size. Although the developed scoring tool is easy to use in EDs, it is not applicable where there is limited access to modern CT scanners. The density of the lesions was not evaluated in the present study, while some other studies have proposed different densities of lesions based on the severity of the infection (33).

Finally, the information about the patients' lung status before COVID-19 onset was not accessible, which has probably affected our findings. It is highly recommended to perform further studies with a large sample size to validate a more accurate scoring tool.

Conclusions

The present study developed a scoring tool for non-critical new-onset COVID-19 patients in EDs based on their CT scan findings and basic demographic data. TSS, in combination with age range and history of at least one comorbidity, at the cut-off point of more than 8, provided a useful measure for predicting adverse outcomes in these patients.

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Authors' contribution

AJ and EK contributed to the study conception and design. Material preparation, data collection and analysis were performed by PB, EA and SB. The first draft of the manuscript was written by EA and SB and it was re-checked by AJ, EK and PB. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

None declared.

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