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Research Article

Chest CT Severity Score, CURB-65 Score and Their Relationship with in-Hospital-Mortality in COVID-19 Patients

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Abstract

Objective: With every new strain of the SARS-CoV-2 spreading on a fast pace across the borders, an easy-to-calculate and reliable scoring system seems invaluable to identify high-risk patients. This study aims to investigate the relationship between CT Severity Score (CTSS) and CURB-65 score with mortality in COVID-19 patients.

Methods: This study was conducted on RT-PCR confirmed COVID-19 patients admitted to a tertiary teaching center during fifth national wave of disease in one of the early disease epicenters in the country. All enrolled patients underwent chest CT scan within first day of admission. CTSS and CURB-65 scores were calculated and assigned to patients, while radiologist was blinded to clinical and laboratory findings, and they were evaluated for their correlation with in-hospital mortality, additively and separately.

Results: Total number of 216 patients (140 males) with a mean age of 56.02 ± 17.34 years (ranging from 4 to 95) were enrolled. We found no significant relationship between CURB-65 score and CTSS (correlation coefficient: 0.065; P: 0.338). CURB-65 scores above 1 was predictive of in-hospital mortality with sensitivity of 56.4% and specificity of 81.9% (P: 0), those for CTSS above 11 were 79.5% and 4 51.5%, respectively (P: 0.001). CURB-65 score >1 and CTSS >11 predicted in-hospital mortality with sensitivity and specificity of 61.5% and 79.7% (P: 0.000). CURB-65 score and CTSS had a higher sensitivity and specificity to predict mortality comparing to each of those separately, but these enhanced statistics were not significant.

Conclusion: CURB-65 score is meaningfully stronger than CTSS to prognosticate in-hospital mortality in patients with COVID-19, and it is not significantly correlated with CTSS.

Keywords: Computed tomography; COVID-19; CT Severity Score; CURB-65; SARS CoV-2.

Introduction

With the global outbreak of COVID-19 and the rapid spread of the new variants of concern, all societies around the world are facing serious problems. On January 30, 2020, the World Health Organization declared the disease a global health emergency [1]. The disease infects the respiratory epithelial cells by targeting the human respiratory system, especially the lower airways [2]. COVID-19 can manifest with symptoms of the upper respiratory system such as coryza, sneezing and sore throat, despite the fact that it mainly involves the lower respiratory tract [3,4].

Covid-19 has no definitive cure to the moment, and this has led to the high prevalence and mortality of this disease which has put a lot of pressure on the world's health care systems [5], specially countries with lower public vaccination coverage.

Reverse Transcription Polymerase Chain Reaction (RT-PCR) assays are widely used to confirm the infection as the standard diagnostic tool for COVID19, but due to the high rate of false positive results and its unavailability in the early stages of the outbreak, radiological examinations, especially chest CT scans, have played a more effective and practical role in early diagnosis and triage, as most pivotal steps to combat the infection. Chest CT can detect early lung infection, assess the severity of the disease and the extent of the chest involvement, and accordingly help in early triage and resource allocation/patient's stratification [6-9].

In addition, the limitations of facilities such as diagnostic kits and the insufficient capacity of intensive care units double the importance of early identification of cases of COVID-19 who are prone to deterioration of general condition in the course of hospitalization. CT scan of the chest is highly sensitive to diagnose COVID-19 and more importantly it is available and fast in this era of resources shortage [10-14]. But CT scan alone cannot be used to rule out or rule in COVID-19 definitely [15].

CURB- 65 score determines the severity of pneumonia, and consists of five variables, each scored zero or 1 (with total score of 0-5), and is widely used to predict the 30-day mortality rate from

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community-acquired lung infections [16].

In an article by Gietema et al., It was found that by adding the CURB-65 score to the CTSS, the accuracy of CT scan in effectively diagnosing or rejecting pneumonia in patients clinically suspected of COVID-19 increases; as CURB-65 score greater than or equal to 3 in conjunction with a suggestive CT scan provides 100% sensitivity for COVID-19 detection [15].

The aim of this study was to determine the relationship between the CTSS and the CURB-65 score in COVID-19 patients and their individual and additive power to predict in-hospital mortality.

Material and Methods

This is an observational study and the data that support the findings of this investigation were collected retrospectively.

Study population

The hard copy and electronic records of all 216 participants with RT-PCR confirmed COVID-19 referred and admitted to our tertiary teaching center from April 2020 and September (fifth wave of outbreak in the country), who underwent on admission chest CT scan, were reviewed. Relevant positive and pertinent negative findings from history, physical examination, and laboratory data of studied patients were collected and recorded by the physician at the time of admission and all participants underwent Chest CT scan within the first 24 hours of admission. Missing pertinent data, including clinical symptoms, underlying diseases, etc., were obtained through telephone contact with patients. Patients with other lung diseases with possibility of presenting with similar manifestations on chest CT scan and potential of disturbing the CT severity scoring system (such as patients suspected for pulmonary edema [according to lesion distribution and opacities with dramatic response to diuretics] or lung contusion/alveolar hemorrhage [suggestive history]), patients with blood culture positive for either community-acquired or nosocomial pneumonia, and patients with artifactual chest CT scans were excluded from our study. In general, 216 subjects (140 men) remained eligible to go under investigation.

Chest CT protocols

All images were obtained on a same CT scanner (Toshiba, Canon, Alexia, Japan, 16-detector) and images were reconstructed in axial plane, with slice thickness of 3 mm, mAS of 100 and kvp of 120-100, while patient in supine position with raised hands. Images were taken at full inspiration (as tolerated by patient), reconstructed with sharp kernel, and reviewed in both mediastinal (WW: 400 HU, WL: 40 HU) and lung windows (WW: 1500 HU, WL: -500 HU).

Chest CT images interpretation

A radiologist confident and experienced in thoracic imaging (with 5 years of experience) interpreted the CT scan images adhering to a systematic approach, and findings were compared to previous reports. A CTSS was assigned to each participant, while radiologist was completely unaware of the clinical and laboratory findings.

Statistical analysis

Raw data was analyzed via SPSS software version 22, using both descriptive (frequency distribution and central indices and dispersion) and inferential statistics (t-test for comparing the mean of quantitative variables, and Chi-square test to assess the correlation between categorical variables). Significant predictors were then identified using the univariate model. In the next step, the multivariate conditional logistic regression model was used to design a model indicating the relationship between considered variables and patients mortality rate. Only variables with a p-value of less than 0.25 were included in the model. The results of the Omnibus test are acceptable model fit and significant at an error level of less than 0.001. After determining the significant predictor(s), the sensitivity and specificity (accuracy) of predicting mortality was measured for the CT-ss alone and with other model predictors through analyzing ROC curves.

Results

In this study, the hard copy and electronic records of 216 patients with rRT-PCR confirmed COVID-19 (140 men) with a mean age of 56.02 ± 17.34 years (ranging from 4 to 95 years) were reviewed. Our results showed that the median onset of symptoms and perform RT-PCR was 5 days [3-7].

Diabetes mellitus (38%), hypertension (28.7%) and cardiovascular diseases (21.3%) were the most common underlying diseases among the subjects. In general, 12.5% of patients had a history of smoking cigarette or hookah. The most common blood group in the subjects was blood type O (42.3%).

Among the symptoms fever (79.2%), weakness and lethargy (65.3%), body aches (59.3%) and dry cough (59.3%) were the most common presenting symptoms on admission. The median scores of CT scan and CURB-65 were 13 (6-24) and 1 (0-75), respectively (Table 1).

Among the patients studied, 21 (9.7%) received adjuvant oxygen during hospitalization, 20 (9.3%) underwent mechanical ventilation, and finally 39 (18.1%) died during hospitalization.

Table 2 shows that although CTSS and CURB-65 score are not significantly correlated (P = 0.338, r= 0.065), but are strongly correlated with age and in-hospital death (p < 0.01).

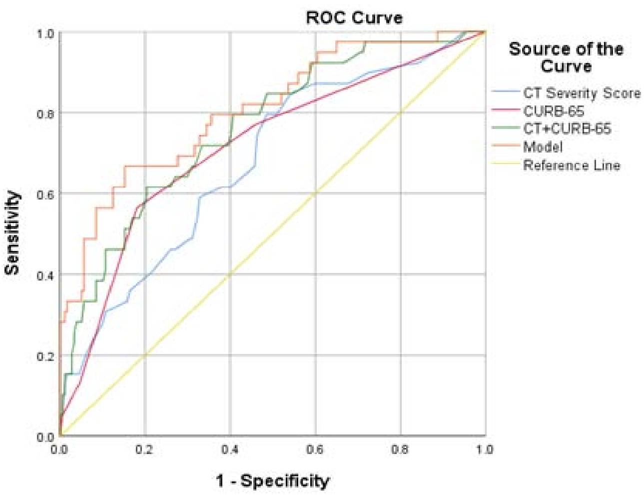

Figure 1: ROC curves for CTSS and CURB-65 scoring system to predict in-hospital mortality.

Table 1: Demographic, clinical, laboratory, and imaging findings and their relationship with the final clinical outcome and CTSS/CURB-65 score in studied patients.

Variable		CTSS	CURB-65 score
Age	F	16 (25/6-24)	0 (0-2)
	M	11 (5-22)	1 (0-1)
	p-value	159/0	621/0
Gender	r (p-value)	179/0 (000/0)	650/0 (000/0)
DM	Y	12 (5-5/22)	1 (0-1)
	N	14 (6-24)	1 (0-2)
	p-value	349/0	616/0
HTN	Y	5/13 (5-24)	5/0 (0-1)
	N	13 (6-5/22)	1 (0-2)
	p-value	882/0	692/0
CVD	Y	5/12 (5-24)	1 (0-2)
	N	14 (6-5/22)	0 (0-1)
	p-value	795/0	021/0
CPD	Y	5/9 (5-75/19)	0 (0-1)
	N	14 (6-24)	1 (0-2)
	p-value	179/0	480/0
CGC	Y	11 (6-24)	1 (0-1)
	N	14 (5/5-24)	1 (0-2)
	p-value	695/0	841/0
Smoking	Y	15 (7-28)	0 (0-1)
	N	13 (5-22)	1 (0-2)
	p-value	262/0	178/0
Blood group	AB	5/12 (25/6-5/19)	1 (0-2)
	A	10 (5-24)	1 (0-1)
	B	9 (2-22)	1 (0-1)
	O	16 (8-24)	0 (0-2)
	p-value	188/0	963/0
Fever	Y	14 (6-24)	1 (0-2)
	N	9 (5/4-5/21)	0 (0-5/1)
	p-value	035/0	369/0
Chills	Y	5/11 (5-5/23)	1 (0-2)
	N	14 (6-24)	0 (0-1)
	p-value	513/0	206/0
Malaise	Y	13 (6-24)	1 (0-2)
	N	13 (5-22)	1 (0-1)
	p-value	479/0	728/0
Myalgia	Y	5/12 (6-5/23)	1 (0-1)
	N	14 (25/5-24)	5/0 (0-2)
	p-value	910/0	881/0
Chest pain	Y	16 (7-24)	0 (0-75/1)
	N	12 (5-22)	1 (0-75/1)
	p-value	227/0	221/0
Dyspnea	Y	5/13 (25/6-22)	1 (0-2)
	N	13 (25/5-24)	1 (0-1)
	p-value	951/0	222/0
Dry cough	Y	5/12 (6-24)	1 (0-2)
	N	14 (25/5-5/23)	0 (0-1)
	p-value	967/0	263/0
Productive cough	Y	10 (25/4-5/23)	0 (0-75/1)
	N	14 (6-24)	1 (0-75/1)
	p-value	282/0	718/0
Headache	Y	14 (5/7-24)	1 (0-1)
	N	12 (5-22)	1 (0-2)
	p-value	244/0	782/0
Dizziness	Y	14 (5/9-23)	1 (0-1)
	N	12 (5-24)	1 (0-2)
	p-value	198/0	663/0
Nausea	Y	12 (5-22)	1 (0-1)
	N	14 (6-24)	0 (0-2)
	p-value	603/0	406/0
Vomiting	Y	13 (6-5/23)	1 (0-1)
	N	13 (25/5-24)	5/0 (0-2)
	p-value	768/0	661/0
Diarrhea	Y	16 (6-24)	1 (0-2)
	N	12 (5-22)	0 (0-1)
	p-value	183/0	221/0
Hemoptysis	Y	10 (5-20)	1 (0-1)
	N	14 (6-24)	1 (0-2)
	p-value	199/0	849/0
Sys BP	r (p-value)	024/0 (722/0)	122/0- (074/0)
Dias BP	r (p-value)	064/0- (351/0)	218/0- (001/0)
RR	r (p-value)	103/0 (133/0)	210/0 (002/0)
WBC	r (p-value)	098/0 (150/0)	232/0 (001/0)
Lymph	r (p-value)	119/0- (082/0)	190/0- (005/0)
Plt	r (p-value)	022/0 (753/0)	009/0 (899/0)
BUN	r (p-value)	039/0 (571/0)	698/0 (000/0)
Cr	r (p-value)	041/0 (547/0)	422/0 (000/0)
PE	Y	11 (7-24)	1 (0-2)
	N	13 (5-24)	1 (0-1)
	p-value	973/0	542/0
CTSS	r (p-value)	-	065/0 (338/0)
O2 therapy	Y	16 (7-22)	0 (0-1)
	N	13 (5-24)	1 (0-2)
	p-value	736/0	111/0
Mechanical ventilation	Y	17 (25/7-30)	1 (0-2)
	N	12 (5-22)	1 (0-1)
	p-value	120/0	665/0
Hospital LOS	r (p-value)	034/0- (615/0)	144/0 (034/0)
In-hospital mortality	Y	18 (12-30)	2 (1-2)
	N	11 (5-22)	0 (0-1)
	p-value	001/0	000/0

BUN: Blood Urea Nitrogen; CGC: Chronic Glucocorticoid Administration; CPD: Chronic Pulmonary Disease; Cr: Creatinine; CTSS: CT Severity Score; CVD: Cardiovascular Disease; Dias BP: Diastolic Blood Pressure; DM: Diabetes Mellitus; F: Female; HTN: Hypertension; LOS: Length of Stay; Lymph: Lymphocyte Count; M: Male; PE: Pleural Effusion; Plt: Platelet Count; r: Regression Coefficient; RR: Respiratory Rate; Sys BP: Systolic Blood Pressure; WBC: White Blood Cell Count.

Additionally, CTSS, unlike CURB-65 scores, were significantly associated with fever on admission ($p = 0.035$); and CURB-65 scores, unlike CTSS, was predictive of cardiovascular disease history, diastolic blood pressure, and respiratory rate. There was a significant relationship between white blood cells, lymphocytes, blood urea nitrogen, creatinine and length of hospital stay ($p < 0.05$).

Afterward, in order to model the relationship between the variables in Table 2 with in-hospital mortality, the multiple logistic regression model was deployed, results of which are presented in (Table 3). Noteworthy, only variables with p-values of less than 0.25 in the simple logistic (univariate) regression were incorporated into the model (the results are not presented due to lack of necessity); Therefore, 17 variables (age, symptoms onset to RT-PCR interval, history of cardiovascular disease, fever, weakness and lethargy,

Table 2: Multiple logistic regression model to predict in-hospital mortality.

Variable	Regression Coefficient	p-value	Odd Ratio (OR)
Hemoptysis	763/1	012/0	829/5
Plt	009/0-	026/0	991/0
BUN	087/0	024/0	091/1
CTSS	048/0	023/0	049/1

Model Info: (488/0, 298/0); Pseudo R^2=436/76; Omnibus Test=p <0.001.
BUN: Blood Urea Nitrogen; CTSS: CT Severity Score; Plt: Platelet Count.

shortness of breath, dizziness, hemoptysis, white blood cell count, lymphocyte count, platelet count, Blood urea nitrogen, creatinine, CTSS, CURB-65 score, mechanical ventilation and length of hospital stay) were included in the multiple regression model.

Table 3 shows that according to the results of the Omnibus test, the model fit is acceptable and at the error level less than 0.001 is significant. Also, the value of the coefficient of determination (Pseudo R-square) shows that mentioned 17 variables are able to explain between 29.8 to 48.8% of the changes in patient mortality. In addition, according to parental statistics values and p-value, it can be implied that out of 17 variables, only 4 variables of hemoptysis, platelet count, blood urea nitrogen and CTSS have a significant relationship with patient mortality.

In order to evaluate the value of CTSS and CURB-65 in predicting in-hospital mortality, ROC curves were plotted, which are presented in Table and the following graph.

According to the results in Table, CURB-65 scores above 1 (with a sensitivity of 56.4% and specificity of 81.9% [p < 0.001, AUC = 0.715]) and CT scan scores above 11 (with a sensitivity of 79.5% Specificity of 51.4% [p < 0.001, AUC = 0.678]) are predictive of in-hospital mortality in COVID-19 patients. It should be noted that the predictive power of both CURB-65 and CTSS was more than that of each of those scores individually, although the difference was not significant. Moreover, the predictive power of the model (hemoptysis + platelet count + blood urea nitrogen + CTSS) was significantly higher than that of CURB-65 score or CTSS as individual factors.

Discussion

With successive global outbreaks of COVID-19, each time a new variant of concern being the culprit, all global societies are facing serious problems. The World Health Organization declared the disease as a global health emergency [1]. There are always ongoing efforts to introduce a prognostic scoring system that can predict the outcome for patients with COVID-19 [17]. In this study we aimed to test the predictive value of CTSS and CURB-65 score, in combination and individually, to predict in-hospital mortality in COVID-19 patients.

Our retrospective study, although did not show a significant relationship between chest CT scan and CURB-65 scores, the predictive power of CURB-65 and CT scan scores for in-hospital mortality was higher when they were implemented in conjunction. In addition, each of the CT scan and CURB-65 scores were significantly associated with age and in-hospital death.

We also found that the most common risk factors for COVID-19 are diabetes mellitus, hypertension and cardiovascular disease, smoking cigarette/hookah, and having blood group O. As in a cross-sectional study of 174 patients with COVID-19 admitted to Wuhan Hospital by Guo et al., Diabetes mellitus was identified as an important risk factor for COVID-19. Another study by Chen et al. showed that previous exposure to cardiovascular disease increased the risk of developing COVID-19 infection [18].

In our study, the most common symptoms of patients on admission were fever, weakness, lethargy, pain, and dry cough. Several studies have been performed on the clinical signs of COVID-19 infection. In a review article on the clinical signs of COVID-19 infection, as in our study, symptoms such as cough, fatigue, shortness of breath, fever, diarrhea, and headache were reported as primary symptoms [19].

CURB-65 score value to estimate the severity of pneumonia is well-known and has been extensively investigated. In an investigation on 1,014 patients in China conducted by Tao et al., CT scan and CURB-65 were significantly associated with in-hospital mortality, which is in keeping with our results. Moreover, a study by Francon et al. reported a potential role for CTSS for predicting the final clinical outcome in SARS-CoV-2 infected patients. In their study, CTSS was highly correlated with laboratory findings and disease severity [20].

Additionally, in our study, CTSS was significantly associated with the presence of on-admission fever while CURB-65 score was not, and CURB-65 scores had a significant association with the history of cardiovascular disease, on-admission diastolic blood pressure, respiratory rate, white blood cell count, lymphocyte count, blood urea nitrogen, creatinine, and length of hospital stay, while CTSS had not. However, in a post-adjusted age-effect study, Guan et al. demonstrated that blood pressure is not a risk factor for COVID-19 [21]. In addition, Tehrani et al. showed that having a history of cardiovascular disease, including myocardial infarction, increases the risk of blood clot formation following COVID-19, which can lead to the death of a patient with COVID-19 [22].

To evaluate the value of CT scan and CURB-65 scores in predicting in-hospital mortality, ROC curves were plotted, which showed that CURB-65 score above 1 was more specific (with a sensitivity of 56.4% and specificity of 81.9%) and CTSS above 11 was more sensitive (with a sensitivity of 79.5% and specificity of 51.4%) for predicting

Table 3: CTSS and CURB-65 scoring system sensitivity and specificity to predict in-hospital mortality, in combination or individually. Cut-offs indicate best point of discrimination between high and low chance of in-hospital mortality.

	Cut-off	Sensitivity (%)	Specificity (%)	AUC	p-value	Confidence Interval
CURB-65 Score	1	56/4	81/9	715/0	000/0	(808/0-621/0)
CTSS	11	79/5	51/4	678/0	001/0	(769/0-586/0)
CURB-65 Score + CTSS	-	61/5	79/7	761/0	000/0	(844/0-678/0)
MLR model	-	67/66	75/84	806/0	000/0	(885/0-727/0)

AUC: Area under the Curve; CTSS: CT Severity Score; MLR: Multivariate Logistic Regression.

in-hospital mortality in hospitalized COVID-19 patients. CURB-65 has also been shown to be useful in predicting 14-day mortality in nosocomial pneumonia [23]. The relationship between CURB-65 score and in-hospital mortality has been reported previously [24,25].

Liu et al. studied 56 patients with COVID-19 and showed that CTSS is averagely higher in elderly patients [26], which is in line with our findings. Previous studies have also shown that adding the CRP value to the CTSS does not increase the predictive power in hospitalized COVID-19 patients [27].

In our study, the predictive power of the CURB-65 score and CTSS together was higher compared to these scores separately; however, the difference was not statistically significant. In a similar study by Gietema et al., it was shown that by adding the CURB-65 score to the CT scan scoring system, the diagnostic accuracy in clinically suspected patients and predictive power in the confirmed cases would increase. They demonstrated that a CURB-65 score greater than or equal to 3 in conjunction with a suggestive CT scan is 100% sensitive to diagnose COVID-19 [15]. Another study on 681 patients By Satici et al. found that the combined predictive power of CT scan and CURB-65 or predictivity of CT scan alone is higher than that of CURB-65 [28]. Nguyen et al. reported a higher predictive value for CTSS and associated it with limited parameters being considered in CURB-65, not including some other important factors, such as underlying disease(s), hypoxia, need for oxygen therapy, D-dimer and IL-6 levels, and myocardial involvement [29].

Our study had some noteworthy limitations. Investigating only hospitalized patients makes it difficult to generalize our data to other patients. Due to the retrospective design, data analysis is subjected to biases, and our data need verification from prospectively designed studies.

Conclusion

Our study found a dependable predictive power for CURB-65 and CT scan score in combination to anticipate in-hospital mortality. Although CTSS and CURB-65 scores were not significantly correlated, they were meaningfully associated with patients' age and in-hospital mortality rate.

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