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Original Article

Association between CHA2DS2-VASc score and in-hospital death in ICU patients with COVID-19

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Abstract

Background: CHA2DS2-VASc score is a scientifically proven risk assessment score for patients with atrial fibrillation. It may be a good predictor of in-hospital death in COVID-19 patients. The present study aimed to evaluate the association between CHA2DS2-VASc score and in-hospital mortality in the prognosis of intensive care unit (ICU) patients with COVID-19.

Methods: Eighty-four COVID-19 patients who were hospitalized in the ICU were retrospectively analyzed in a tertiary health care center, and the CHA2DS2-VASc score was determined. All analyses were performed using SPSS statistical software (SPSS Inc., Chicago, IL, USA, 20.0). A p-value <0.05 was considered statistically significant.

Results: The median age of patients was 60.0 years, and most were males (75.0%). Findings of the study showed that the CHA2DS2-VASc score was considerably higher among the hospitalized patients than discharged patients (3.08 ± 1.72 vs. 1.38 ± 1.16; p<0.001), and patients who required mechanical ventilation compared to those who did not require mechanical ventilation (3.03 ± 1.68 vs. 1.15 ± 0.97; P <0.001), respectively. Patients with CHA2DS2-VASc score of ≥3 had substantially higher age [67(45-87) vs. 58(19-75); P <0.001], computed tomography involvement score [67.5(20-90) vs. 35(15-90); P <0.001] and need for mechanical ventilation [29(90.6%) vs. 22(42.3%); P <0.001]. A significant difference was found in oxygen saturation on admission (P =0.001) between the two groups. In-hospital death was significantly higher among patients with a CHA2DS2-VASc score of ≥3 (P <0.001). The CHA2DS2-VASc score was positively correlated with white blood cells count (r=0.257, P =0.018) and negatively correlated with the number of days spent in the hospital (r=-0.184, P=0.130) due to higher in-hospital death in ICU patients with COVID-19.

Conclusion: CHA2DS2-VASc score may be an effective tool to estimate in-hospital death in COVID-19 patients who were hospitalized in the ICU.

Keywords: COVID-19, CHA2DS2-VASc, In-Hospital Death, Intensive Care Unit, SARS-CoV-2, India

Background

Coronavirus disease 2019 (COVID-19), a highly contagious disease due to a new type of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), had emerged in December 2019 in Wuhan, Hubei province, China. This unique coronavirus disease has created an outbreak of uncommon viral pneumonia due to its high transmissibility, which poses an extraordinary threat to public health worldwide [1]. COVID-19 had spread to over 200 countries, resulting in more than 240 million identified cases with more than 49 lakhs confirmed deaths on October 22, 2021 [2]. Several risk factors like elderly age, males,

hypertension, diabetes mellitus, previous cardiovascular disease, and high neutrophil-lymphocyte ratio are linked to death in COVID-19 patients [3-5]. Acute respiratory distress syndrome [6], cardiac injury [7, 8], venous thromboembolism, and arterial thrombosis [9] are several complications of COVID-19. The CHA2DS2-VASc (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes mellitus, prior stroke or transient ischemic attack [doubled], vascular disease, age 65-74 years, and sex category [female]) is a scientifically proven risk assessment score used to estimate the peril of ischemic stroke in patients with atrial fibrillation [10], and also predicts mortality in several cardiovascular diseases [11]. Many of the risk factors of CHA2DS2-VAScscore are also predictive risk factors for morbidity and mortality in COVID-19 [12]. So far, there is a dearth of literature on the relationship between

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CHA2DS2-VASc score and COVID-19 patients [13, 14]. Therefore, the current study determined the association between the CHA2DS2-VASc score and prognosis of intensive care unit (ICU) patients with COVID-19 infection in terms of in-hospital death.

Methods

Study population

This was a single-center, retrospective study comprising consecutive 84 COVID-19 patients who were hospitalized in the ICU of Sri Aurobindo Medical College and P.G. Institute between December 2, 2020, and February 18, 2021. The diagnosis of COVID-19 was performed based on the World Health Organization's interim guidance.

Inclusion and exclusion criteria

Patients (age >18) with laboratory-confirmed COVID-19 by chest computed tomography or real-time reverse transcription-polymerase chain reaction (RRT-PCR) (using both nasopharyngeal and throat swab samples) examinations were included. Exclusion criteria were patients with serious liver disease, hereditary coagulation disorders, active cancer, chemotherapy–radiotherapy treatment, malignancy, and immunodeficiency. Patients were safely discharged if they met the following criteria: a) absence of fever last for three days, b) improvement in chest computed tomography, c) clinical disappearance of respiratory symptoms, as well as d) negative result in RT-PCR detection of SARS-CoV-2 RNA.

Questionnaire

Baseline demographics, clinical examination, and relevant investigations reports like white blood cells (WBC) count, C-reactive protein (CRP), D-dimer, ferritin, and lactate dehydrogenase (LDH) were consecutively obtained from patients' medical records. The CHA2DS2-VASc score was determined based on their echocardiographic and demographic characteristics and includes the following clinical characteristics: + 1 point for each factor like congestive heart failure, hypertension, diabetes mellitus, vascular disease, age between 65 and 74 years, and female gender and + 2 points for each factor like age ≥75 years and previous stroke/transient ischemic attack [10]. The study population was segregated into two groups based on CHA2DS2-VASc score [group I: CHA2DS2-VAScscore <3 (n=52); group II: CHA2DS2-VASc score ≥3 (n=32)].

Statistical analysis

Descriptive data are represented as mean ± SD for continuous variables with a normal distribution, median (interquartile range [IQR]) for continuous variables with a non-normal distribution, and frequency (%) for categorical variables. The Shapiro-Wilk test was used to test the normality of the distribution of continuous variables. The independent t-test and the Mann-Whitney U test were used to compare continuous variables with normal and non-normal distributions as appropriate. Chi-square or Fisher exact tests were used to compare categorical variables as appropriate. Pearson's correlation coefficient was used to assess the linear correlation between two variables. A 2-tailed p-value <0.05 was considered statistically significant. All analyses were performed using SPSS statistical software, version 20.0 (Statistical Package for Social Sciences, Inc., Chicago, Illinois, USA).

Results

Sociodemographic factors

A total of 84 COVID-19 patients who were hospitalized in the ICU [median age: 60.0 years (range: 54.3–68.8 years); males: 63 (75.0%)] were included in the study. Of the 84 patients, diabetes was the most frequent presentation [45(53.6%) patients], followed by hypertension [40(47.6%) patients]. Based on CHA2DS2-VASc score, the number of patients in grade 0, 1, 2, 3, 4, 5, 6, 7 was 14, 13, 25, 15, 6, 4, and 1 respectively. The clinical profile of study patients is outlined in Table 1.

Table 1 Clinical profile of study patients (n = 84)

Patient characteristics	Total (n=84)
Age (years)	60.0(54.3-68.8)
Male	63(75.0%)
CT-IS	50.0(30.0-73.8)
WBC count on admission	9500.0(6875.0-13375.0)
Need for mechanical ventilation	51(60.7%)
Duration of hospital stay (days)	8.0(5.0-10.8)
CHA2DS2-VASc score components	
Age <65 (years)	47/84(56.0%)
Age 65–74 (years)	25/84(29.8%)
Age ≥75 (years)	12/84(14.2%)
Female	21/84(25.0%)
Past medical history	
Heart Failure	11/84(13.1%)
Hypertension	40/84(47.6%)
Stroke/TIA/T.E.	8/84(9.5%)
Vascular disease/MI/PAD	11/84(13.1%)
Diabetes	45/84(53.6%)
CHA2DS2-VASc score	
0	14/84(16.7%)
1	13/84(15.5%)
2	25/84(29.8%)
3	15/84(17.9%)
4	6/84(7.1%)
5	6/84(7.1%)
6	4/84(4.8%)
7	1/84(1.2%)
Other morbidities	
Acute respiratory distress syndrome	1/19(5.3%)
Chronic kidney disease	5/19(26.3%)
Chronic obstructive pulmonary disease	1/19(5.3%)
HBsAg +	2/19(10.5%)
Hepatitis B +	1/19(5.3%)
Hypothyroidism	4/19(21.1%)
Hypothyroidism/AKI/Sepsis	1/19(5.3%)
Pancreatitis	1/19(5.3%)
Post CABG	1/19(5.3%)
Relapsed non-Hodgkin lymphoma	1/19(5.3%)
Sickle cell disease	1/19(5.3%)
Oxygen saturation on admission (%)	
<85%	49/84(58.3%)
>85%	35/84(41.7%)
Inflammatory markers on admission	
CRP (mg/dL)	
Normal<0.6 mg/Dl	27/84(32.1%)

Abnormal	57/84(67.9%)
D Dimer (µg/mL)	
Normal<200 µg/Ml	49/84(58.3%)
Abnormal	35/84(41.7%)
Ferritin (ng/mL)	
Normal (10-291 ng/mL)	23/84(27.4%)
Abnormal	61/84(72.6%)
LDH (U/L)	
Normal (313-618 U/L)	39/84(46.4%)
Abnormal	45/84(53.6%)
Status	
Discharged	39/84(46.4%)
Hospitalized	45/84(53.6%)

AKI-acute kidney injury; CABG-coronary artery bypass grafting; CHA2DS2VASc-congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category; CRP-C-reactive protein; CT-IS-CT involvement score; HBsAg-hepatitis B surface antigen; LDH-lactate dehydrogenase; MI-myocardial infarction; PAD-peripheral artery disease; TE-systemic thromboembolism; TIA-transient ischemic attack; WBC- white blood cells. Data are presented as median (interquartile range) or n (%).

Comparison of clinical characteristics of study patients based on CHA2DS2-VASc score is outlined in Table 2. The enrolled patients were allocated to the group I (n=52) and group II (n=32). Age was considerably higher in group 2 [67(45-87)] than group I [58(19-75)] (P=<0.001). Patients in group II had substantially higher CT INV [67.5(20-90) vs. 35(15-90); p= <0.001] and higher need for mechanical ventilation [29(90.6%) vs. 22(42.3%); p= <0.001] as compared to group 1. Significant differences were found in oxygen saturation on admission (p=0.001) and status of the patients (hospitalized, discharged) (p=<0.001) between the two groups. Association of total CHA2DS2-VASc score with patients' status need of mechanical ventilation and oxygen saturation on admission was also evaluated. The CHA2DS2-VASc score was considerably higher in hospitalized patients than in discharged patients (3.08 ± 1.72 vs. 1.38 ± 1.16; p=<0.001). Moreover, this score was substantially higher in patients who required mechanical ventilation than those who did not (3.03 ± 1.68 vs. 1.15 ± 0.97; p=<0.001). On admission, CHA2DS2-VASc score was non-significantly higher in the measured oxygen saturation<85% than >85% (2.63 ± 1.81 vs. 1.82 ± 1.46; p=0.02).

Table 2: Comparison of clinical characteristics of study patients based on CHA2DS2VASc score (n = 84)

Patient characteristics	Total CHA2DS2VASc score		p-value
	< 3 (n=52)	**≥ 3 (n=32)**	
Age (years)	58(19-75)	67(45-87)	**<0.001**
CT INV	35(15-90)	67.5(20-90)	**<0.001**
WBC count on admission	8300(3300-23100)	11000(4400-32000)	0.013
Need for mechanical ventilation	22(42.3%)	29(90.6%)	**<0.001**
Duration of stay (days)	8(1-21)	6.5(1-15)	0.216
Oxygen saturation on admission (%)			
<85%	23(44.2%)	26(81.2%)	**0.001**
>85%	29(55.8%)	6(18.8%)	
Inflammatory markers on admission			
CRP (mg/dL)			
Normal<0.6 mg/Dl	18(34.6%)	9(28.1%)	0.536
Abnormal	34(65.4%)	23(71.9%)	
D Dimer (µg/mL)			
Normal<200 µg/mL	30(57.7%)	19(59.4%)	0.879
Abnormal	22(42.3%)	13(40.6%)	
Ferritin (ng/mL)			
Normal (10-291 ng/mL)	16(30.8%)	7(21.9%)	0.375
Abnormal	36(69.2%)	25(78.1%)	
LDH (U/L)			
Normal (313-618 U/L)	25(48.1%)	14(43.8%)	0.699
Abnormal	27(51.9%)	18(56.2%)	
Status			
Hospitalized	19(36.5%)	26(81.2%)	**<0.001**
Discharged	33(63.5%)	6(18.8%)	

CHA2DS2-VASc-congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category; CRP-C-reactive protein; LDH-lactate dehydrogenase; WBC-white blood cells

As shown in Table 3, no significant association was found between the total CHA2DS2-VASc score with inflammatory markers on admission. There was a significant positive correlation found between CHA2DS2-VASc score and WBC count (r=0.257, p=0.018), whereas the number of days spent in hospital (r=-0.184, p=0.130) was negatively correlated with the CHA2DS2-VASc score, but the association was found to be non-significant (Figure 1 and 2).

Discussion

The COVID-19 is more severe in patients with underlying cardiovascular diseases such as complicated myocardial injury, myocarditis, congestive heart failure, thromboembolism, and arrhythmias [15]. There is a lack of a widely accepted scoring system for risk prediction in COVID-19 patients. However, the CHA2DS2-VASc score is a scientifically proven risk assessment score for determining the risk of thromboembolism, ischemic stroke, and mortality in patients with atrial fibrillation[10].

Table 3: Comparison of inflammatory markers on admission with total CHA2DS2-VASc score (n = 84)

Inflammatory markers on admission	Total CHA2DS2VASc score	p-value
CRP (mg/dL)		
Normal<0.6 mg/dL, n=27	2.00 ± 1.54	0.358
Abnormal, n=57	2.43 ± 1.78	
D Dimer (µg/mL)		
Normal<200 µg/mL, n=49	1.91 ± 1.71	0.006
Abnormal, n=35	2.82 ± 1.58	
Ferritin (ng/mL)		
Normal (10-291 ng/mL), n=23	2.08 ± 1.92	0.294
Abnormal, n=61	2.37 ± 1.63	
LDH (U/L)		
Normal (313-618 U/L), n=39	2.23 ± 1.49	0.883
Abnormal, n=45	2.35 ± 1.89	

CHA2DS2-VASc-congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category; CRP-C-reactive protein; LDH-lactate dehydrogenase; SD-standard deviation; WBC-white blood cells. Data are represented as mean ± SD.

Additionally, this score can also predict mortality and the need for ICU hospitalization in COVID-19 patients [13]. However, there is a lack of data on the correlation between CHA2DS2-VASc score and in-hospital morality in COVID-19 patients who were hospitalized in the ICU [14, 16, 17]. In the retrospective study of ICU patients with COVID-19, we aimed to investigate the association between the CHA2DS2VAScscore and the prognosis of ICU patients with COVID-19 in terms of hospital mortality. The significant findings were as follows: a) ICU patients with COVID-19 having CHA2DS2-VASc score ≥3 was found at high risk of death; b) higher CHA2DS2-VAScscore was associated with a smaller number of hospitalization days due to higher morality; c) higher the CHA2DS2-VAScscore, higher the WBC count.
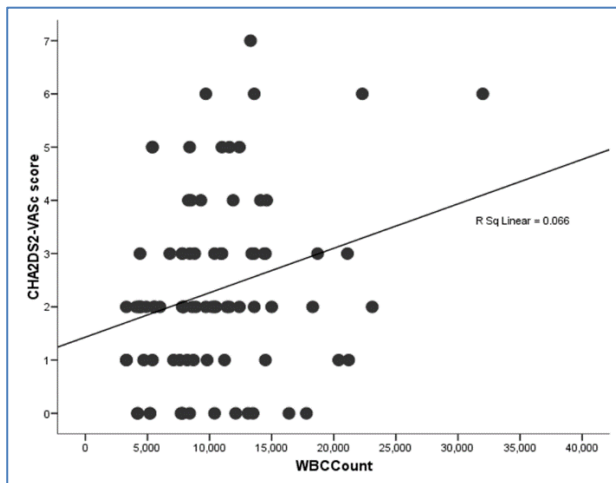
total population had underlying worse clinical conditions such as cardiovascular or cerebrovascular diseases. Likewise, many studies reported that 32% [6], 46.4% [19], and 40% [20] of the COVID-19 patients who were hospitalized in the ICU had underlying cardiovascular diseases, respectively. The development of coagulopathy adversely affects the prognosis of the COVID-19 patients. Following parameters should be assessed to detect coagulopathy: D dimer, platelet count, prothrombin time, and fibrinogen level; as an increased level of D-dimer, massive fibrin formation, CRP, ferritin levels, and leukocytes count on hospital admission are associated with poor prognosis, extended mechanical ventilation, as well as higher in-hospital death [21-23]. In our study, a higher incidence of more severe systemic inflammation, including higher levels of CRP, ferritin, and LDH on admission, was associated with higher in-hospital death in COVID-19 patients. Owing to the fact that the severity of COVID-19 is also based upon the severe systemic inflammation, data pertaining to the D-dimer, massive fibrin formation, CRP, ferritin levels, LDH, and leukocytes count on hospital admission is of paramount importance. The present study found higher CHA2DS2-VASc scores in hospitalized COVID-19 patients than in discharged COVID-19 patients. This may be the reason for the higher incidence of invasive mechanical ventilation, high levels of oxygen saturation, high levels of WBC counts, and shorter duration of hospital stay recorded in the patients with hospitalized patients. This finding is in accordance with findings reported by Quasi et al.[14]. Another study by Cetinkal et al.[24] also stated that the COVID-19 infection was much more severe in the patients with higher CHA2DS2-VASc scores. Based on this, the CHA2DS2-VASc score may be an independent predictor of in-hospital death in COVID-19 patients who were hospitalized in the ICU.
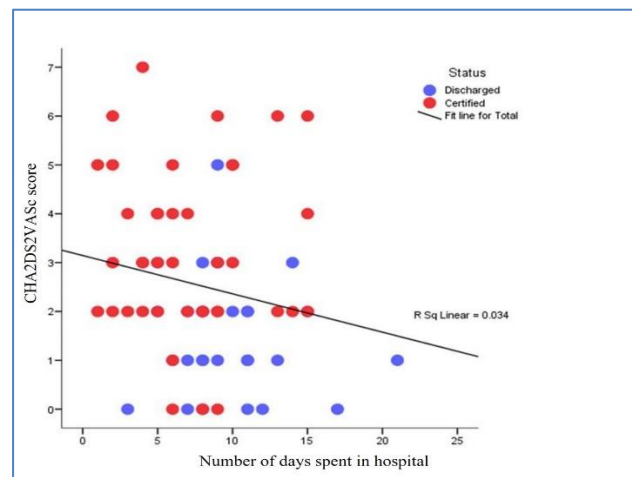

Figure 1: Correlation between CHA2DS2VASc score and WBC count. CHA2DS2-VASc-congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category; WBC-white blood cells.

Figure 2. Correlation between CHA2DS2VASc score and number of days spent in hospital. CHA2DS2VASc-congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category.

Most of the CHA2DS2-VASc score variables have also emerged as prognostic risk factors in COVID-19 patients hospitalized in the ICU [12]. The present study demonstrated that COVID-19 patients had worse clinical conditions, such as elderly age and higher diabetes mellitus and hypertension. Similar to our study, Chen et al. [18] also found that 40% of the

The design of this study entails some constraints. First, this was a retrospective study with a small sample size. Second, information regarding medications used by patients with hypertension, diabetes, and other diseases was not included. Lastly, in-hospital morality was only reported due to the retrospective nature of the study. Association of CHA2DS2-

VASc scores with in-hospital death of ICU patients with COVID-19 warrants further investigation.

Conclusion

Assessment of CHA2DS2-VASc score can help clinicians for estimating in-hospital death in ICU patients with COVID-19. Our study showed overall high CHA2DS2-VASc scores in the hospitalized patients and further noted that a CHA2DS2-VASc score of ≥3 on hospital admission predicted in-hospital death in ICU patients with COVID-19. Therefore, CHA2DS2-VAScscore can decrease the peril of deleterious events during hospitalization of high-risk COVID-19 patients and allow improvement in patients' management. However, more studies are needed to confirm these findings.

Abbreviation

CHA2DS2-VASc: congestive heart failure, hypertension, age ≥75 years [doubled], diabetes mellitus, prior stroke or transient ischemic attack [doubled], vascular disease, age 65-74 years, and sex category [female], COVID-19: Coronavirus disease 2019, CRP: C-reactive protein, ICU: intensive care unit, IQR: interquartile range, LDH: lactate dehydrogenase, RRT-PCR: real-time reverse transcription-polymerase chain reaction, SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, WBC: white blood cells.

Declaration

Acknowledgment

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Availability of data and materials

Data will be available by emailing dr.mukeshjha@hotmail.com.

Authors' contributions

All authors equally contributed to the concept, design, literature search, data analysis, and data acquisition, manuscript writing, editing, and reviewing.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. The ethical protocol was approved by the Institutional Ethics Committee of Sri Aurobindo Medical College and P.G. Institute (Reg. No.: SAIMS/IEC/2021/20) and adhered to the tenets of the Declaration of Helsinki. Moreover, each patient has given written informed consent during the treatment for properly anonymized clinical data usage.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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