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Research Article

Evaluation of Relationship between Modified ATRIA Risk Score and Mortality in Hospitalized Patients with COVID-19

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Abstract

Aim: The ATRIA score was developed to assess the probability of an ischemic stroke in patients with atrial fibrillation (AF). The modified ATRIA (M-ATRIA) risk score incorporates predictive risk variables for coronavirus disease 2019 (COVID-19). As a result, we looked into the association between the M-ATRIA risk score and the risk of in-hospital death in COVID-19 patients.

Materials and Methods: The data of 595 inpatients in the COVID-19 research were evaluated retrospectively and separated into three groups based on the M-ATRIA scoring system. The M-ATRIA score used the troponin I level as a parameter in place of the proteinuria criterion in the ATRIA score. Those with a score between 0 and 5 were classified as group 1 (n = 269), those with a score of 6 as group 2 (n = 64), and those with a score of 7 and above were classified as group 3 (n = 162). In-hospital death, mechanical ventilation, and admission to the critical-care unit were all considered adverse clinical events.

Results: The M-ATRIA risk score associated with adverse clinical events (all, $p < 0.001$). An M-ATRIA score of 6, an M-ATRIA score greater than 7, procalcitonin, and C- reactive protein were found to be independent predictors of in-hospital mortality in the multivariate logistic regression analysis. In the ROC analysis, an M-ATRIA score of 4.5 or above predicted in-hospital mortality with a sensitivity of 90.2% and a specificity of 58.9%.

Conclusion: Regardless of the status of AF, the M-ATRIA risk score computed at admission may be a valuable tool for predicting in-hospital mortality in COVID-19 patients.

Keywords: Coronavirus disease 2019, M-ATRIA risk score, intensive care unit, in-hospital mortality

INTRODUCTION

Even though the vaccine has been available for roughly two years, intensive care unit (ICU) admissions and significant fatality rates are still linked with coronavirus disease 2019 (COVID-19) (1). Most significantly, it affects the respiratory system and causes severe acute respiratory distress syndrome (ARDS). However, arterial thrombosis and venous thromboembolism may also occur during COVID-19 infection secondary to endothelial injury and hypercoagulability (2).

In order to predict the risk of thromboembolism and guide the start of anticoagulant medication in patients with atrial fibrillation (AF), the risk scores CHADS2, CHA_2DS_2-VASc, and ATRIA were developed. In two grand population-based cohort researches, the ATRIA stroke risk score was shown to predict thromboembolic events better than the CHA_2DS_2-VASc and $CHADS_2$ risk scores in non-COVID-19 populations (3,4). Hypertension (HT), diabetes mellitus (DM), older age, chronic heart failure (CHF), and prior ischemic stroke are all components of these three risk scores. In hospitalized COVID-19 patients, these comorbidities raise death and morbidity rates (5). Higher CHA_2DS_2-VASc risk scores at the time of hospitalization were observed to predict in-hospital death in COVID-19 patients (5,6).

Prognostic COVID-19 risk indicators are included in the ATRIA risk score. There are very few studies carried out the association between in-hospital mortality and ATRIA risk score in COVID-19 patients. Proteinuria is a component of the ATRIA risk score, but now that it is not routinely obtained on admission in COVID-19 patients, we excluded this variable from the score calculation. Because greater troponin I levels are linked to an increased mortality rate in COVID-19 patients (7), we developed a modified ATRIA (M-ATRIA) risk score by replacing the proteinuria criterion with troponin I. There is no data in the literature to our knowledge about the value of the newly generated M-ATRIA

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score in predicting the prognosis of COVID-19 patients when the proteinuria criterion in the ATRIA risk score is altered with troponin I. The study's goal was to examine the relation between death and the M-ATRIA risk score in hospitalized COVID-19 patients, irrespective of AF status.

MATERIAL AND METHOD

Study population

The medical data of 555 individuals who presented to our tertiary hospital's emergency department and were hospitalized with COVID-19 between December 1, 2020 and January 1, 2021 were reviewed retrospectively. Data from the physical examination, clinical assessment, laboratory workup, and chest computed tomography (CT) imaging were obtained for all patients. Nasopharyngeal swab samples were collected from all patients by healthcare professionals at the time of hospital admission. Those with a positive PCR (Polymerase Chain Reaction) test result were considered as confirmed COVID-19 cases. Those with a negative PCR test result received treatment for COVID-19 and were comprised in the study if chest CT scans showed typical signs of COVID-19 infection. These included unilateral or bilateral sub-segmental, multiple patchy, or segmental/lobar ground-glass opacities within the lung that could not be explained by another cause or condition (8). All patients were diagnosed with COVID-19 as per the WHO interim guidance on COVID-19, and the decision to admit the patient was in accordance with national guidelines (8).

COVID-19 patients with dyspnea, a respiratory rate > 30/min, hypotension, a heart rate of >100 bpm, PaO_2<70 mmHg, PaO_2/FiO_2<300, immunosuppression, acute organ dysfunction, sepsis, increased troponin level, septic shock, need for mechanical ventilation (MV), acute bleeding diathesis, and arrhythmia were admitted to the ICU. Comorbidities (prior cerebrovascular diseases, CHF, HT, DM, AF, chronic obstructive lung disease, status renal disease, cardiovascular diseases, and prior malignancy), demographic characteristics, treatment protocols, mortality data, radiographic findings, and laboratory parameters were retrieved from the hospital electronic medical record. Laboratory parameters, obtained within the first 24 hours of admission, were also used in the study. Patients who had missing or incomplete laboratory data and terminal cancer patients were excluded. Data from the initial admission were used in the study for the 12 patients who had undergone several hospitalizations in the previous month.

Patients with lung CT findings and PCR tests that did not suggest Covid-19 (n=35), incomplete laboratory data (n=20), and patients with terminal cancer (n=5) were excluded from the study. This retrospective cohort analysis included 495 patients (55.6% males, n=275), with an average age of 67.6±14.7 years.

Patients who presented with neurological symptoms that persisted for more than 24 hours and imaging techniques revealed ischemia or bleeding in the brain, were diagnosed as stroke. Transient ischemic attack was characterized as a temporary neurological dysfunction lasting less than 24 h with associated symptoms. Hypertension was regarded as having a blood pressure of ≥ 140/90 mmHg or being treated for HT. Having DM was based on having a fasting blood glucose level of ≥126 mg/dL or having DM by diagnosis. CHF was described by a left ventricular ejection fraction of <40%. eGFR was calculated as follows:

$186 * (age - ^{0.203}) * (plasma\ creatinine\ ^{-1.154}) * (0.742\ if\ female)$

Ethics statement: Approval was acquired from Clinical Research Ethics Committee for the current study. (Date: 16/02/2021, Decision no: 2021/02-11). The research adheres to the Declaration of Helsinki Principles

Scoring system

Prior ischemic stroke and older age are the two most significant risk variables for the ATRIA scoring algorithm. This scoring system was adapted in this study (Table 1). For patients without prior stroke, scoring according to age is done as follows; ≥85: 6 points, 75-84: 5 points, 65-74: 3 points, <65: 0 points. For patients with a prior stroke, scoring according to age is done as follows; 85: 9 points, 65-84:7 points, <65: 8 points. In addition, 1 point each was assigned for female gender, DM, CHF, HT and eGFR< 45 mL/min/1.73 m^2 irrespective of prior stroke (3).

Table 1. Risk factors used in Modified ATRIA Risk Score

Risk factors	Points without prior stroke (points)	Points with prior stroke (points)
Age, years		
>85	6	9
75–84	5	7
65-74	3	7
<65	0	0
Female sex	1	1
Chronic heart failure	1	1
Diabetes mellitus	1	1
Hypertension	1	1
eGFR <45 mL/min/1.73 m^2 or ESRD	1	1
*Troponin I	1	1

ESRD: end-stage renal disease
* Elevated troponin I (> 0.023 ng/mL) was assigned a score of 1

The proteinuria feature of the original ATRIA score was purposefully replaced with troponin I to improve the prediction of death in COVID-19 patients because increased troponin I is known to be a significant predictor of mortality in hospitalized patients due to COVID-19 (7). Elevated troponin I (> 0.023 ng/mL) was assigned a score of 1. This new score was designated as the modified ATRIA (M-ATRIA) score.

The study population was divided into three groups based on the M-ATRIA risk score due to the stratification of the ATRIA score into high (7 to 15 points), moderate (6 points), and low (0 to 5 points) risk categories (3). Group 1 had scores ranging from 0 to 5 (n = 269), Group 2 had scores ranging from 6 to 64, and Group 3 had scores ranging from

7 to 162. As adverse clinical outcomes, admission to the ICU, invasive MV, and in-hospital mortality were identified.

Statistical analysis

In the study, the minimum total sample size was determined according to a power of 0.85 with moderate effect size. An additional 15% more of power analysis was included in the research. Numerical data distribution was determined by the Kolmogorov-Smirnov test. Baseline parameters were displayed as median (quartile deviation) or mean ± standard deviation, and categorical variables were offered as numbers and percentages. The Kruskal-Wallis test with post-hoc analysis (Dunn's test) was used to evaluate continuous variables, while Pearson's chi-squared test was used to analyze categorical variables. In the univariate binary logistic regression analysis, predictors were those thought to be closely associated to in-hospital mortality. To exclude statistically non-significant predictors and avoid a multicollinearity problem, forward variable selection was applied to the predictors in the multivariate binary logistic regression analysis.

The model's fit was evaluated using the Hosmer-Lemeshow test. Each independent variable's odds ratio (OR) and 95% CI were calculated. Kaplan-Meier curves were also plotted. To explore the relation between in-hospital survival and M-ATRIA score groups, the log-rank test was used. Finally, using the Youden's Index to assess in-hospital mortality, the analysis of receiver operating characteristic (ROC) curve was used to determine the ideal cutoff value for the M-ATRIA scores, troponin I, and C-reactive protein (CRP) levels. Statistically significant difference was regarded as a p value less than 0.05. Statistical computations were carried out using SPSS (v23.0, IBM Corp., Chicago, IL, USA) and R software (version 4.0.5 R Core Team).

RESULTS

In the study population, the mortality rate was 24.6% and the likelihood of admission to an ICU was 28.5%. Table 2 lists the demographic characteristics and comorbidities of the study sample, stratified by M-ATRIA risk scores. There were no significant differences in malignancy, length of hospital stay, or chronic lung disease across the groups (all p>0.05). Patients who have the high M-ATRIA score were older with a higher frequency of CHF, DM, HT, cerebrovascular disease, chronic kidney disease, elevated troponin I, reduced eGFR, coronary artery disease (all, p<0.001), and AF (p=0.005). From a low M-ATRIA tertile or score to a high M-ATRIA tertile or score, in-hospital mortality, ICU admission, and MV rose progressively (all, p<0.001). Group I had an in-hospital mortality rate of 9.7%, Group 2 had a rate of 29.7%, and Group 3 had a rate of 47.5%. Except for favipravir treatment (p=0.021), inpatient treatments were comparable among the three groups.

Table 2. Comorbidities and demographic features of the study population

	Group 1: M-ATRIA= 0-5 (n=269)	Group 2: M-ATRIA= 6 (n=64)	Group 3: M-ATRIA ≥7 (n=162)	p-value
Age (years)	59 (8)	75.7 ± 6.4	80 (6.0)	**<0.001***
M-ATRIA score components				
Age ≥85, n (%)	0 (0 %)	4 (6.3 %)	50 (30.9 %)	**<0.001**
Age 75-84, n (%)	11 (4.1 %)	38 (59.4 %)	84 (51.9 %)	**<0.001**
Age 65-74, n (%)	77 (28.6 %)	20 (31.3 %)	22 (13.6 %)	**0.001**
Age <65, n (%)	181 (67.3 %)	2 (3.1 %)	6 (3.7 %)	**<0.001**
Female, n(%)	99 (36.8 %)	24 (37.5 %)	97 (59.9 %)	**<0.001**
Chronic heart failure, n (%)	4 (1.5 %)	11 (17.2 %)	37 (22.8 %)	**<0.001**
Diabetes mellitus, n (%)	65 (24.2 %)	22 (34.4 %)	68 (42.0 %)	**<0.001**
Serebrovascular disease, n (%)	2 (0.7 %)	2 (3.1 %)	39 (24.1 %)	**<0.001**
Hypertension, n (%)	90 (33.5 %)	26 (40.6 %)	124 (76.5 %)	**<0.001**
Increase in troponin I, n (%)	25 (9.3 %)	14 (21.9 %)	55 (34.0 %)	**<0.001**
eGFR<45, n (%)	15 (5.6 %)	17 (26.6 %)	46 (28.4 %)	**<0.001**
Chronic lung disease, n (%)**	60 (22.3 %)	20 (31.3 %)	45 (27.8 %)	0.223
Chronic kidney disease, n (%)	16 (5.9 %)	13 (20.3 %)	34 (21.0 %)	**<0.001**
Coronary artery disease, n (%)	50 (18.6 %)	16 (25 %)	94 (58.0 %)	**<0.001**
Malignancy, n (%)	19 (7.1 %)	10 (15.6 %)	14 (8.6 %)	0.092
Atrialfibrillation, n (%)	9 (3.3 %)	6 (9.4 %)	18 (11.1 %)	**0.005**
Length of hospitalstay, days	8 (3.5)	10.5 (5.5)	9 (5.0)	0.050
Treatments, n (%)				
Favipiravir	241 (89.6 %)	58 (90.6 %)	157 (96.9 %)	**0.021**
Antibiotics	253 (94.1 %)	60 (93.8 %)	152 (93.8 %)	0.993
Glucocorticoids	269 (100 %)	64 (100 %)	162 (100 %)	-
Mechanicalventilation, n (%)	20 (7.4 %)	14 (21.9 %)	47 (29 %)	**<0.001**
Admissionto ICU, n (%)	53 (19.7 %)	21 (32.8 %)	67 (41.4 %)	**<0.001**
In-hospitalmortality, n (%)	26 (9.7 %)	19 (29.7 %)	77 (47.5 %)	**<0.001**

* p<0.001 between Group 1 and 2, p<0.001 between Group 1 and 3, p= 0.102 between Group 2 and 3; **Chronic lung disease was defined as choronic obstructive pulmonary disease, chronic bronchitis or asthma; eGFR; estimated glomerular filtration rate, ICU; intensive care unit.

Table 3 displays the laboratory results of the patients enrolled in the study. Urea, creatinine, CRP, procalcitonin and fibrinogen levels increased as the M-ATRIA score or tertile increased (all, p<0.05). On the other hand, the levels of hemoglobin, eGFR, and albumin declined from a higher to a lower M-ATRIA tertile or score (all, p<0.001). Patients with low M-ATRIA tertiles or scores had lower levels of troponin I and D-dimer than patients with high and intermediate M-ATRIA tertiles or scores (all, p<0.001).

Table 3. Risk factors used in Modified ATRIA Risk Score

	Group 1: M-ATRIA= 0-5 (n=269)	Group 2: M-ATRIA= 6 (n=64)	Group 3: M-ATRIA ≥7 (n=162)	p-value	Post-Hoc Analysis p-value
Hæmoglobin, g/dL	13.9 (1.1)	13.2 ± 2.4	12.8 ± 1.2	**<0.001***	**Group 1 vs 2:** 0.092 **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.562
Platelet count, (×10³/μL)	217.0 (55.5)	185.0 (60)	202.5 (59.6)	**0.021***	**Group 1 vs 2: 0.025*** **Group 1 vs 3:** 0.372 **Group 2 vs 3:** 0.444
White blood cell count, (×10³/μL)	7.6 (2.2)	7.7 (3.9)	8.7 (3.2)	0.130	
Procalcitonin, ug/L	0.2 (0.1)	0.2 (0.1)	0.3 (0.3)	**0.001***	**Group 1 vs 2:** 0.092 **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.562
Serum creatinine, mg/dl	0.9 (0.2)	1 (0.4)	1.1 (0.4)	**<0.001***	**Group 1 vs 2:** 1.000 **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.233
eGFR, mL/min/1.73 m²	83.1 (21.9)	74.7 (21.0)	60.4 (17.6)	**<0.001***	**Group 1 vs 2: <0.001*** **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.060
Urea, mg/dL	31.0 (10.0)	50.5 (26.2)	53.0 (25.5)	**<0.001***	**Group 1 vs 2: <0.001*** **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.699
Alanine aminotransferase, U/L	27.0 (11.0)	22.5 (10.3)	22.0 (9.6)	**0.003***	**Group 1 vs 2:** 0.101 **Group 1 vs 3: 0.005*** **Group 2 vs 3:** 1.000
Aspartat aminotransferase, U/L	34.0 (11.5)	33.5 (14.8)	37.5 (14.3)	0.709	
Albumin, g/dL	3.3 (0.4)	2.9 (0.4)	3.0 (0.3)	**<0.001***	**Group 1 vs 2: 0.007*** **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 1.000
Fibrinogen, g/L	495.4 (94.0)	496.7 (92.5)	538 (116.3)	**0.037***	**Group 1 vs 2:** 0.092 **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.562
C-reactive protein, mg/dL	7.0 (4.4)	8.8 (3.7)	8.9 (5.5)	**0.004***	**Group 1 vs 2:** 1.000 **Group 1 vs 3: 0.045*** **Group 2 vs 3:** 0.227
D-Dimer, μg/L	986.0 (421.3)	1425 (654.2)	1350 (670.5)	**<0.001***	**Group 1 vs 2: 0.007*** **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 1.000
Troponin I, μg/L	0.01 (0.00)	0.01 (0.00)	0.01 (0.03)	**<0.001***	**Group 1 vs 2: 0.031*** **Group 1 vs 3: <0.001*** **Group 2 vs 3:** 0.319

*P value <0.05; eGFR: Estimated glomerular filtration rate

In order to evaluate the independent determinants of in-hospital mortality, logistic regression analysis was utilized. According to the results of the multivariate logistic regression analyses, the COVID-19 patients' M-ATRIA score of 6 (OR, 3.598; 95%CI, 1.748–7.404; p=0.001), M-ATRIA score of 7 (OR, 6.825; 95%CI, 3.977–11.883; p<0.001), procalcitonin (OR,1.957; 95%CI, 1.370–2.94; p<0.001), and the CRP level (OR,1.100; 95% CI, 1.061–1.141; p<0.001) were all independently predictive factors for in-hospital death (Table 4).

Table 4. Univarite and Multivariate Binary Logistic Regression Analysis to Identify the Predictors of in Hospital Mortality

Univarite	OR	95% Confidence interval	p-value	Multivariate	OR	95% Confidence interval	p-value
M-ATRIA score groups			<0.001	M-ATRIA score groups			<0.001
M-ATRIA 6	3.946	(2.016-7.724)	<0.001	M-ATRIA 6	3.598	(1.748-7.404)	0.001
M-ATRIA ≥7	8.467	(5.091-14.079)	<0.001	M-ATRIA ≥7	6.875	(3.977-11.883)	<0.001
Age (years)	1.060	(1.041-1.079)	<0.001		1.100	(1.061-1.141)	<0.001
Sex (male)	1.380	(0.909-2.096)	0.130	Procalsitonin	1.957	(1.370-2.794)	<0.001
Troponin I	27.470	(8.960-84.214)	<0.001	Constant	0.032	-	<0.001
C-reactive protein	1.120	(1.084-1.157)	<0.001				
Procalsitonin	2.710	(1.909-3.848)	<0.001				

The ROC curve analysis showing the predictive accuracy of CRP, troponin I, and the M-ATRIA risk score for in-hospital mortality is displayed in Figure 1. ROC curve analysis showed that a CRP level of 11.8 mg/dL had a sensitivity of 56.6% and a specificity of 78.2% in predicting in-hospital mortality, whereas a troponin I value of 0.019 µg/L had a sensitivity of 58.2% and a specificity of 93%. An M-ATRIA score of 4.5 and over had a sensitivity of 90.2% and a specificity of 58.9% for the prediction of in-hospital mortality (area under curve [AUC] 0.70, 0.76, 0.80, respectively). Figure 2 displays the Kaplan-Meier survival curves based on M-ATRIA scores. Mortality significantly increased in patients with a higher M-ATRIA score (p<0.001 by the log-rank test). Significantly higher survival rates were seen in patients with M-ATRIA risk scores under 6.

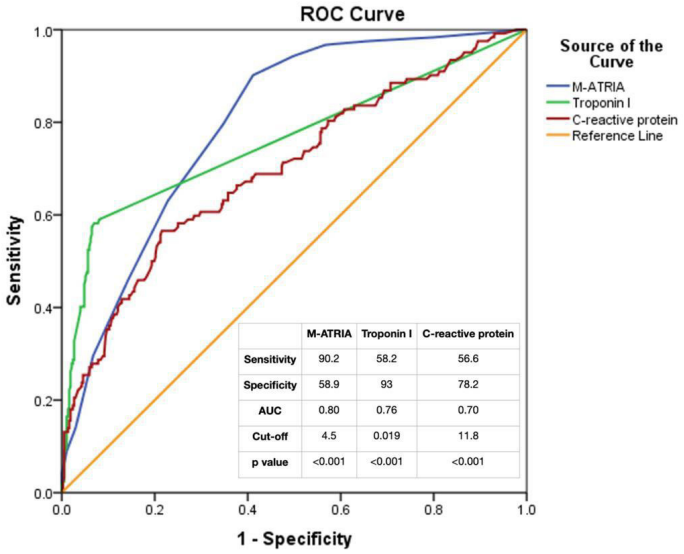
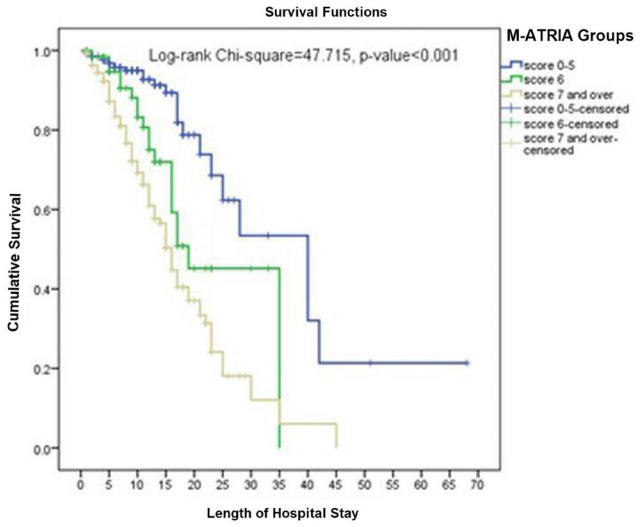


Figure 1. ROC analysis showing the predictive accuracy of Troponin-I, M-ATRIA score, and C-reactive protein for in-hospital mortality.
AUC: Area under the curve



Means and Medians for Survival Time

M-ATRIA GROUPS	Mean Estimate	Mean Std. Error	Mean 95% Confidence Interval Lower Bound	Mean 95% Confidence Interval Upper Bound	Median Estimate	Median Std. Error	Median 95% Confidence Interval Lower Bound	Median 95% Confidence Interval Upper Bound
score 0-5	36.644	4.590	27.648	45.640	40.000	6.761	26.749	53.251
score 6	22.914	2.130	18.740	27.089	19.000	3.176	12.775	25.225
score7 and over	17.682	1.362	15.012	20.352	16.000	0.876	14.284	17.716
Overall	25.923	2.048	21.910	29.937	22.000	1.530	19.000	25.000

Figure 1. ROC analysis showing the predictive accuracy of Troponin-I, M-ATRIA score, and C-reactive protein for in-hospital mortality.

DISCUSSION

The results of the study showed that, independent of AF status, the M-ATRIA score predicted in-hospital mortality in COVID-19 hospitalized patients. Patients with a higher M-ATRIA score also had increased rates of adverse events. In addition, the ROC curve analysis affirmed the prognostic performance of the M-ATRIA score.

COVID-19 primarily impresses the respiratory tract, but can also lead to multi-organ dysfunction and is related to high mortality rates and ICU admission. Although the in-hospital

mortality among patients in ICU is lower compared to the initial stages of the pandemic, it remains high (35.5%) (9). As a result, predicting in-hospital mortality of COVID-19 patients on admission is crucial for devising a treatment strategy and reducing adverse events. Elevated troponin I levels, an indicator of myocardial injury, have been linked to higher in-hospital mortality in this population (7). Similarly, elevated troponin I was an independent and strong indicator of in-hospital mortality in this study. The risk scoring prediction of M-ATRIA for in-hospital mortality was improved by substituting the troponin I levels measured at admission for the evidence of proteinuria in the ATRIA risk score.

Advanced age, a factor in the M-ATRIA score, is linked to higher rates of morbidity and mortality in COVID-19 patients. Age-related increases in COVID-19-related hospital mortality and ICU admissions (10). In high-income countries, individuals under 65 years of age have a 16 to 100-fold lower risk of death from COVID-19 compared to those over 65 years of age (11). In a meta-analysis of COVID-19 reports published until May 7, 2020, mortality rates of 9.5% in patients aged 60 to 69 years, 22.8% in patients aged 70 to 79 years, and 29.6% in patients over the age of 80 were reported (12). A separate study reported a mortality rate of 38.8% among hospitalized individuals with COVID-19 over the age of 85 (13). Thus, risk scores that include particularly high-risk elderly individuals can be used to predict mortality while managing the pandemic.

In a study involving 349 COVID-19 patients, non-survivor patients had a higher CHA_2DS_2-VASc score versus the survivor group. It has been shown to be an independent predictor of death to have a score of three or higher (6). Cetinkal ve ark. (5) examined the link between the CHA_2DS_2-VASc score on admission and mortality in patients with COVID-19. The researchers arbitrarily altered the sex category from female to male and showed that their modified CHA_2DS_2-VASc score predicted in-hospital mortality independently. Ruocco et al. (13) discovered that the CHA_2DS_2-VASc score was an independent predictor of in-hospital mortality in a study of 864 COVID-19 patients.

Similar variables are included in the ATRIA and CHA_2DS_2-VASc risk score models. The ATRIA risk score system is more detailed than the CHA_2DS_2-VASc risk score system in terms of age. For example, when calculating the CHA_2DS_2-VASc score, all age groups over the age of 75 are assigned the same score, whereas in the ATRIA risk scoring, individuals aged ≥ 85 years are assigned a higher score than those aged ≥ 75 years. This may increase the power of the ATRIA score to predict mortality of COVID-19 patients. Additionally, renal dysfunction, a variable linked to a higher mortality in COVID-19 patients, is also included in the ATRIA score (14). This confers greater power to the score for predicting mortality. Aciksari et al. (15) reported in their study that the M-ATRIA risk score predicted in-hospital death in individuals hospitalized due to COVID-19 (AUC:0.74). In the current study, the M-ATRIA score predicted in-hospital mortality (AUC: 0.80). In contrast to their work, adding the troponin value to the M-ATRIA score increased test discriminative power in our study.

Other components of the M-ATRIA score, such as DM, heart failure, prior stroke, and low eGFR, have been linked to higher in-hospital mortality in COVID-19 patients, according to studies (5-7). Likewise, comorbidities were more common in patients with a higher M-ATRIA score in our study. Although the underlying mechanism for increased severity and mortality observed in patients with comorbidities has not been elucidated, a number of factors were implicated, such as an impaired immune system, low-grade inflammation, and an elevated level of angiotensin converting enzyme 2 (ACE-2) receptors (16-18).

Arterial and venous thrombotic events (i.e, pulmonary embolism, acute limb ischemia, deep venous thrombosis, acute mesenteric ischemia, acute myocardial infarction, ischemic stroke) due to immobilization, hypoxia, hypercoagulability, and endotheliosis are a prominent reason of increased mortality and morbidity in patients with COVID-19 (19). Patients experience poor outcomes despite the administration of adequate anticoagulant therapy (20). Thrombotic complications were observed more frequently in elderly patients with comorbidities (21). A meta-analysis of 20 studies involving 1.988 patients reported a venous thromboembolism prevalence of 31% (22). In a meta-analysis of 27 studies examining arterial thrombotic events in COVID-19 patients, about 4.4% of critically ill COVID-19 patients admitted to ICU developed arterial thrombosis (21). In a recent meta-analysis of 42 studies, Malas et al. (23) reported that both venous and arterial thromboembolism rates were high in COVID-19 patients and thromboebolism was associated with a high risk of mortality. Caro-Codón et al. (20) reported that the modified CHA_2DS_2-VASc and CHA_2DS_2-VASc scores anticipate all-cause mortality in COVID-19 patients. The researchers reported that 3.8% of patients presented with a definite thrombotic event, and these scores do not predict thromboembolic events. Therefore, according to the findings of our study, it may be speculated that there is a relationship between M-ATRIA score and COVID-19 mortality.

The ATRIA score is a validated risk score model that has been improved to foretell the thromboembolism risk for AF patients. In non-valvular AF, endothelial dysfunction, local/systemic inflammation, and hypercoagulability play a role in thrombus formation (3,4). Although thrombosis in COVID-19 patients occurs through the same mechanisms, the main underlying pathophysiology is thrombo-inflammation induced by excessive immune activation and cytokine storm (2).

Risk prediction models have been developed for disease progression, ICU admission, and death in COVID-19 patients. Most models are web-based risk scores or nomogram models consisting of clinical, laboratory and radiological components (24,25). When externally validated, some of the risk prediction models were found to be weak in predicting mortality. El-Solh et al.

(26) performed external validation of four risk prediction models to anticipate mortality among COVID-19 patients in a large cohort. The authors noted that all of the prognostic models showed poor performance and a high risk of bias. In COVID-19 patients, the M-ATRIA score of admission time may be utilized as a practical and simple tool to predict in-hospital mortality. The variables that are incorporated into the score also predict mortality, and thromboembolic complications increase mortality.

Limitations of the Study

Now that the study had a retrospective design, the comorbidity status of the participants may not have been fully captured. Adequate imaging studies for ischemic/embolic events may be lacking because of the prioritization of isolation protocols and to prevent the spread of infection. Since we could not determine the exact number of patients experiencing ischemic/embolic events, we were not able to peruse the association between the M-ATRIA score and ischemic/embolic events. In addition, the CHA_2DS_2-VASc scores of the patients were not calculated, and therefore we could not compare the two scores. Also, in contrast to the CHA_2DS_2-VASc, the ATRIA score model does not include vascular disease as a parameter, which is familiar to be associated with mortality.

CONCLUSION

We determined that the M-ATRIA score may be utilized to recognize patients with a high mortality risk on admission. During the COVID-19 pandemic, making simple, practical scores available to clinicians may be helpful in decision-making and reducing adverse events for high-risk patients requiring ICU monitoring in rapidly deteriorating COVID-19 patients. Prospective studies on larger patient populations are warranted to corroborate our findings.

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REFERENCES

1. Xu S, Huang R, Sy LS, et al. COVID-19 Vaccination and Non-COVID-19 Mortality Risk - Seven Integrated Health Care Organizations, United States, December 14, 2020-July 31, 2021. MMWR Morb Mortal Wkly Rep. 2021;70:1520-24.
2. Godoy LC, Goligher EC, Lawler PR, et al. Anticipating and managing coagulopathy and thrombotic manifestations of severe COVID-19. CMAJ. 2020;192:E1156-61.
3. Singer DE, Chang Y, Borowsky LH, et al. A new risk scheme to predict ischemic stroke and other thromboembolism in atrial fibrillation: the ATRIA study stroke risk score. J Am Heart Assoc. 2013;2:e000250.
4. Van Den Ham HA, Klungel OH, Singer DE, et al. Comparative performance of ATRIA, CHADS2, and CHA_2DS_2-VASc risk scores predicting stroke Comparison of the ATRIA, CHADS2, and CHA_2DS_2-VASc stroke risk scores 3209in patients with atrial fibrillation in a national primary care database and the impact on treatment decisions. J Am Coll Cardiol. 2015;66:1851-9.
5. Cetinkal G, Kocas BB, Ser OS, et al. Assessment of the Modified CHA_2DS_2VASc Risk Score in Predicting Mortality in Patients Hospitalized With COVID-19. Am J Cardiol. 2020;135:143-9.
6. Quisi A, Alıcı G, Harbalıoğlu H, et al. The CHA_2DS_2-VASc score and in-hospital mortality in patients with COVID-19: A multicenter retrospective cohort study. Turk Kardiyol Dern Ars. 2020;48:656-63.
7. Al Abbasi B, Torres P, Ramos-Tuarez F, et al. Cardiac Troponin-I and COVID-19: A Prognostic Tool for In-Hospital Mortality. Cardiol Res. 2020;11:398-404.
8. The Republic of Turkey Ministry of Health. COVID-19 (SARS-CoV-2 Infection) (Study of Scientific Board) General Information, Epidemiology and Diagnosis.2020. Website https://covid19.saglik.gov.tr/Eklenti/39061/0/covid-19rehberieriskinhastatedavisipdf.pdf accessed date 9 November 2020].
9. Armstrong RA, Kane AD, Kursumovic E, et al. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. Anaesthesia. 2021;76:537-48.
10. Cohen JF, Korevaar DA, Matczak S, et al. COVID-19–Related Fatalities and Intensive-Care-Unit Admissions by Age Groups in Europe: A Meta-Analysis. Front.Med. 2021;7:560685.
11. Ioannidis JPA, Axfors C, Contopoulos-Ioannidis DG. Population-level COVID-19 mortality risk for non-elderly individuals overall and for non-elderly individuals without underlying diseases in pandemic epicenters. Environ Res. 2020;188:109890.
12. Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The Effect of Age on Mortality in Patients With COVID-19: A Meta-Analysis With 611,583 Subjects. J Am Med Dir Assoc. 2020;21:915-8.
13. Ruocco G, McCullough PA, Tecson KM, et al. Mortality Risk Assessment Using CHA(2)DS(2)-VASc Scores in Patients Hospitalized With Coronavirus Disease 2019 Infection. Am J Cardiol 2020;137:111-7.
14. Ozturk S, Turgut alp K, Arici M, et al. Mortality analysis of COVID-19 infection in chronic kidney disease, haemodialysis and renal transplant patients compared with patients without kidney disease: a nationwide analysis from Turkey. Nephrol Dial Transplant. 2020;35:2083-95.
15. Aciksari G, Cetinkal G, Kocak M, et al. Evaluation of Modified ATRIA Risk Score in Predicting Mortality in Hospitalized Patients with COVID-19. Am J MedSci. 2021;S0002-9629:00214-7.
16. Oyelade T, Alqahtani J, Canciani G. Prognosis of COVID-19 in patients with liver and kidney diseases: an early systematic review and meta-analysis. Trop Med Infect Dis. 2020;5:80.
17. Ejaz H, Alsrhani A, Zafar A, et al. COVID-19 and comorbidities: Deleterious impact on infected patients. J Infect Public

Health. 2020;13:1833-9.

18. Rajpal A, Rahimi L, Ismail-Beigi F. Factors leading to high morbidity and mortality of COVID-19 in patients with type 2 diabetes. J Diabetes. 2020;12:895-908.
19. Gerotziafas GT, Catalano M, Colgan MP, et al. Scientific Reviewer Committee. Guidance for the Management of Patients with Vascular Disease or Cardiovascular Risk Factors and COVID-19: Position Paper from VAS-European Independent Foundation in Angiology/Vascular Medicine. ThrombHaemost. 2020;120:1597-628.
20. Caro-Codón J, Lip GYH, Rey JR, et al. Prediction of thromboembolic events and mortality by the CHADS2 and the CHA_2DS_2-VASc in COVID-19. Europace. 2021;23:937-97.
21. Cheruiyot I, Kipkorir V, Ngure B, et al. Arterial Thrombosis in Coronavirus Disease 2019 Patients: A Rapid Systematic Review. Ann Vasc Surg. 2021;70:273-81.
22. Di Minno A, Ambrosino P, Calcaterra I, et al. COVID-19 and Venous Thromboembolism: A Meta-analysis of Literature Studies. SeminThromb Hemost. 2020;46:763-71.
23. Malas MB, Naazie IN, Elsayed N, et al. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: A systematic review and meta-analysis. EClinicalMedicine. 2020;29:100639.
24. Liang W, Liang H, Ou L, et al. China Medical Treatment Expert Group for COVID-19. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. JAMA Intern Med. 2020;180:1081-9.
25. Acar HC, Can G, Karaali R, et al. An easy-to-use nomogram for predicting in-hospital mortality risk in COVID-19: a retrospective cohort study in a university hospital. BMC Infect Dis. 2021;21:148.
26. El-Solh AA, Lawson Y, Carter M, et al. Comparison of in-hospital mortality risk prediction models from COVID-19. PLoS ONE. 2020;15:e0244629.