Original Article

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Evaluation of the ATRIA and CHA2DS2-VASc Scores and Their Performance on Predicting Mortality in Patients with Acute Pulmonary Embolism

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Abstract

Aim: Pulmonary embolism (PE) is a condition caused by thrombosis and is a common cause of death. Although there are studies of PE with CHA2DS2-VASc (C: congestive heart failure or left ventricular systolic dysfunction, H: hypertension, A: age of ≥75 years, D: diabetes mellitus, S: previous stroke, V: vascular disease, A: age between 65 and 74 years, Sc: female gender) and PE severity index (PESI) scores, there is no data on Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) score in PE or comparison of CHA2DS2-VASc and ATRIA scores in PE. We investigated whether ATRIA and CHA2DS2-VASc scores can predict PE and mortality in cases of PE.

Methods: One hundred ninety-eight patients with PE and two hundred eighty controls between July 2017 and July 2021 were included in this retrospective study. Patients' data was provided from the hospital's digital system. Patients' PESI, ATRIA, and CHA2DS2-VASc scores were calculated, and in-hospital mortality was determined as the primary end-point.

Results: The mean age of the patients was 63.9±13.1 years. The frequency of male patients in the PE group was higher (p=0.04), but this difference was invalid in patients with PE who developed primary end-point (p=0.177). ATRIA and CHA2DS2-VASc scores were higher in the PE group (p<0.01 and p=0.02, respectively) and in patients who reached end-point (p=0.001 and p=0.004, respectively). A moderate-high correlation was found between the PESI score and the ATRIA and CHA2DS2-VASc scores (r=0.664, p<0.001, and r=0.484, p<0.001) in the PE group. Pairwise comparison of ROC curve analysis revealed that PESI, ATRIA, and CHA2DS2-VASc scores were not superior to each other in predicting mortality.

Conclusion: Both ATRIA and CHA2DS2-VASc scores are simple, easily calculated risk scores as an alternative to the PESI score in predicting mortality in PE.

Keywords: Hospital mortality, pulmonary embolism, risk factors

Introduction

Pulmonary embolism (PE) is an emergency clinical status with a mortality rate of 25-30% if untreated (1). Even in those who are treated, 8-10% death and 5-20% recurrence are observed (2). Although sudden onset of dyspnea is the most common symptom, patients may also present with atypical chest pain or presyncope/syncope (3,4). Massive emboli, which may be accompanied by findings such as hypotension, shock, cardiac arrest, or right ventricular failure, constitute less than 5% of all PE (5). Many scoring systems have been developed that can predict the presence of PE, prognosis, and mortality, if any (6-8). Wells clinical scoring and Modified Geneve scoring are generally used to evaluate the probability of PE, while the PE severity index (PESI) score, which consists of 11 clinical criteria, is designed to be used to estimate the 30-day end-points (9-12).

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The most important factor in the pathogenesis of PE is thrombosis, which occurs in the deep veins at a rate of 90%, that is, the mechanism is the increase in thrombogenicity (13). Considering this information, it can be thought that the CHA2DS2-VASc (C: congestive heart failure or left ventricular systolic dysfunction, H: hypertension, A: age of ≥75 years, D: diabetes mellitus, S: previous stroke, V: vascular disease, A: age between 65 and 74 years, Sc: female gender) and anticoagulation and risk factors in atrial fibrillation (ATRIA) risk scores, which were mainly developed to predict the risk of stroke in atrial fibrillation patients, are associated with the presence and prognosis of PE. Although there are studies of PE with CHA2DS2-VASc and PESI scores, there is no data on ATRIA score in PE or comparison of CHA2DS2-VASc and ATRIA scores in PE.

This study aimed to investigate the relationship between CHA2DS2-VASc and ATRIA scores and PE risk and end-point in patients with PE and compare these two scores and PESI score in mortality.

Methods

Ethical Standards and Study Design

The study protocol was approved by the Adana City Training and Research Hospital Clinical Research Ethics Committee with the date 14.7.2021 and number 1492 and complies with the research ethics in the Helsinki statement. Participants were included in the study after their consent was obtained.

One hundred and ninety-eight patients with PE diagnosed with computed tomography (CT) angiography were analyzed retrospectively in this study as the study group, and 280 patients who had definitively excluded PE by CT angiography as the control group. Patients' medical history, laboratory data, and the baseline characteristic properties were recorded from the hospital digital system and national health information portfolio. Systolic heart failure (HF) was defined as a left ventricular ejection fraction <40%. Hypertension (HT) was deemed 140/90 mmHg or higher (or 150/90 mmHg or higher if you're over the age of 80). A fasting blood glucose value above 126 mg/dL on at least 2 tests was defined as diabetes mellitus (DM). A stroke is defined as a neurological deficit caused by an acute focal injury to the central nervous system caused by a vascular cause. Patients with a diagnosis of coronavirus 19, a history of PE or deep vein thrombosis, hematological disease, chronic liver disease, autoimmune and/or rheumatological disease, and missing laboratory results in their files were excluded from the study. In-hospital mortality was determined as the primary end-point.

Laboratory Analysis

From venous blood samples, D-dimer and C-reactive protein (CRP) levels of all patients, troponin values, and complete blood counts were analyzed.

Calculation of PESI, ATRIA, and CHA2DS2-VASc Scores

The PESI score has been validated to assess the probability of 30 and 90 day mortality post PE and is calculated by using mdcalc.com/pesi-pulmonary-embolism-severity-index (14).

The ATRIA risk score was calculated by adding 1 point for each of the following factors: female sex, DM, congestive HF, HT, proteinuria, and renal dysfunction (i.e., estimated glomerular filtration rate<45 mL/min/1.73 m^2 or end-stage renal disease) and by adding 0-9 points depending on the specific score weighting of patients' age according to the presence or absence of prior ischemic stroke (15). The CHA2DS2-VASc score was calculated by adding 1 point each for congestive HF, HT, DM, vascular disease, age 65 to 75 years, or female sex, and 2 points each for age ≥75 years or past stroke/transient ischemic attack (16).

Statistical Analysis

All statistical analyses were performed using SPSS 17 (SPSS, Inc., Chicago, Illinois, USA). The Kolmogorow-Smirnov test was used to determine whether continuous variables have a normal distribution or not. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as numbers and percentages. The Student's t-test and Mann-Whitney U test were used to analyze the continuous variables between groups, and categorical variables were compared using the χ^2 test or Fisher's Exact test. Correlations between variables were analyzed using the Pearson correlation test and Spearmen test, if appropriate. Pairwise comparison of receiver operating characteristics (ROC) curve analysis was used to determine the sensitivity and specificity of the ATRIA and CHA2DS2-VASc scores in showing PE and mortality. The results were stated as relative risk and a 95% confidence interval. A $p<0.05$ was considered significant.

Results

This study consisted of 478 consecutive patients with a mean age of 63.9±13.1 years, 57.5% of whom were males. One hundred and ninety-eight of them had PE (8 patients had massive PE, 26 patients submassive PE, and 164 patients non-massive PE) detected in CT angiography and included in the PE group, and the remaining 280 patients were included in the non-PE group. The baseline characteristics and laboratory results of the groups are summarized in Table 1. The number of males in the PE group was higher than the ones in non-PE, and it was

statistically significant (p=0.04). The PE and non-PE groups were similar in terms of DM, HT, HF, and coronary artery disease (p>0.05, all). D-dimer, CRP, brain natriuretic peptide (BNP), WBC, neutrophil, lymphocyte, and troponin levels were higher in the PE group. Twenty-one patients (10.6%) reached the primary end-point in the PE group. Although the frequency of HF was higher in the mortality subgroup, it did not reach the level of significance (14.2% and 3.3%, p=0.057). Other demographic properties were similar between the mortality and non-mortality subgroups. The demographic characteristics and laboratory results of the mortality and non-mortality subgroups are summarized in Table 2.

Mean PESI, ATRIA and CHA2DS2-VASc scores were all different between PE and non-PE group (p<0.001 for PESI and ATRIA scores and p=0.02 for CHA2DS2-VASc score). In the PE group, the mortality-subgroup had the highest values of PESI, ATRIA and CHA2DS2-VASc scores with means of 129.5±40.2, 5.2±2.1 and 3.0±1.2, respectively.

In correlation analysis, a moderate-high correlation was found between the PESI score and the ATRIA and CHA2DS2-VASc scores (r=0.664, p<0.001, and r=0.484, p<0.001) in the PE group (Figure 1).

ROC curve analysis showed that ATRIA score with a cut-off value >3 had sensitivity of 48.99%, specificity of 70.40% and AUC=0.596, p<0.001 and CHA2DS2-VASc score with a cut off value >1 had sensitivity of 70.71%, specificity of 41.60% and AUC=0.568, p=0.01 predicted the PE and furthermore, pairwise comparison of ROC curve analysis revealed that ATRIA score was non-inferior to CHA2DS2-VASc score with a difference between AUC 0.0285, z statistics 1.757 and p=0.078 in predicting PE (Figure 2).

ATRIA score with a cut-off value greater than 4 had a sensitivity of 66.67%, specificity of 66.67% and AUC=0.716, p<0.001 and CHA2DS2-VASc score with a cut off value >2, sensitivity of 71.43%, specificity of 61.02% and AUC=0.685, p<0.001 and PESI score with a cut off value >108, sensitivity of 76.2%, specificity 59.7% and AUC=0.706, p=0.002 predicted mortality in the PE group. We found that ATRIA, CHA2DS2-VASc and PESI scores were all similar in predicting mortality in the PE group in pairwise comparison of ROC curve analysis (Table 3, Figure 3).

Discussion

We evaluated the association of the ATRIA and CHA2DS2-VASc scores with PE and mortality in PE. The most important results of this study were: 1) ATRIA and CHA2DS2-VASc scores were higher in the PE group compared to the non-PE group, 2) there was a moderate-high correlation between ATRIA and CHA2DS2-VASc scores and the PESI score in the PE group; 3) the highest values of ATRIA and CHA2DS2-VASc scores were in the mortality sub-group in the PE group; and 4) ATRIA, CHA2DS2-VASc and PESI scores were non-inferior to each other in predicting mortality in the PE. These results were the first in the literature to present an association of ATRIA and CHA2DS2-VASc scores with PE and PESI scores.

PE is a common condition with a high mortality rate. The mortality rate is up to 60% in massive PE accompanied

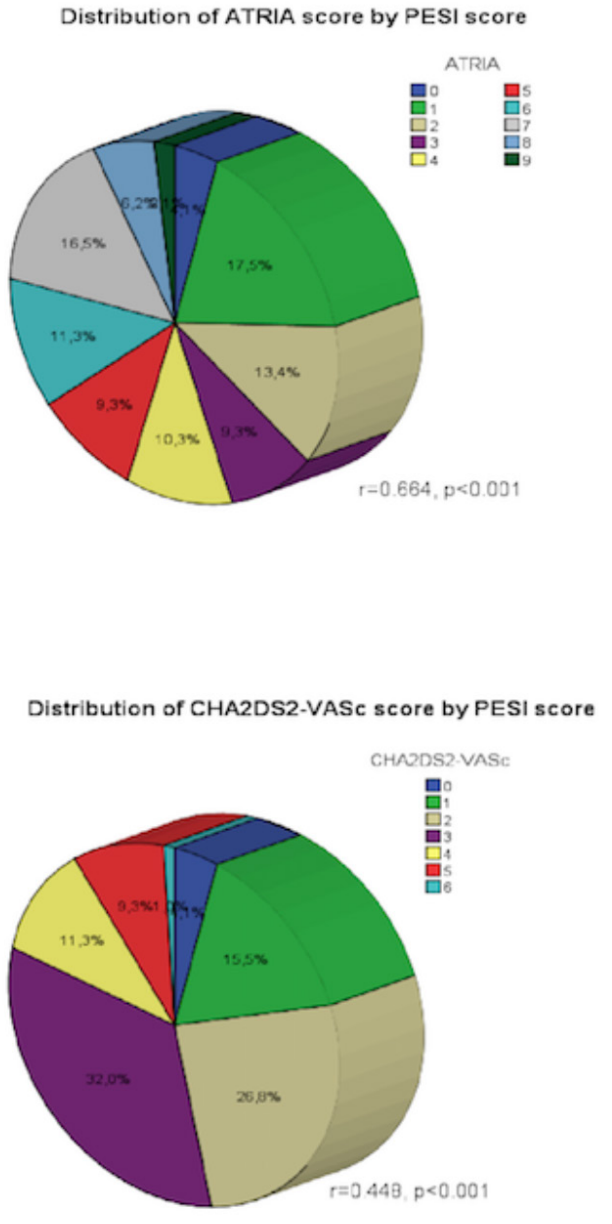

Figure 1. Distribution of ATRIA and CHA2DS2-VASc scores by PESI score

PESI: Pulmonary embolism severity index, ATRIA: Anticoagulation and risk factors in atrial fibrillation

by hemodynamic impairment (17-19). Even in non-massive PE without right ventricular dysfunction and hypotension, 10% of patients may die (20). In this study, death was observed in 5 (62.5%) of 8 patients with massive PE and 10 (6%) of those with non-massive PE. To date, many clinical entities, laboratory parameters, and scoring systems that determine the presence and prognosis of PE have been introduced or developed. The presence of hypotension and shock, the detection of right ventricular dysfunction in echocardiography, and elevated levels of biomarkers such as troponin, pro-BNP, and D-dimer all indicate poor prognosis (21-25). Many studies have shown that inflammation is the main mechanism in the pathogenesis of PE, and inflammatory markers such as higher neutrophil and platelet counts, higher NLR and PLR ratios, and lower levels of lymphocytes have diagnostic importance in PE (26,27). We also obtained results that support these data in our study.

The most commonly used scoring systems for the diagnosis and prognosis of PE are the Wells, revised Geneva, and PESI scores. Angriman et al. (28) reported that a high Wells score determines death and prognosis in PE. Choi et al. (29) revealed that the PESI score predicts mortality, and Guo et al. (30) determined that the Wells score is more diagnostic than the revised Geneva score in elderly patients, and the combination of these scores with D-dimer is safe to exclude PE (29). In contrast to these studies, Li et al. (31) found that cancer-specific PE/VTE scores outperformed the traditional PESI score in identifying low-risk patients with cancer. Furthermore, it was shown in the study by Girardi et al. (32) that Wells and Geneva scores could not predict PE in critically ill patients. These studies reveal the necessity of developing new scoring systems or adapting existing ones in addition to classical scores.

Risk factors for venous thromboembolism, the most common cause of PE, are also components of the CHA2DS2-VASc score. In a study on this subject, Gök et al. (33) revealed that the CHA2DS2-VASc score can predict right ventricular dysfunction in patients with PE. Onuk et al. (34) also stated that the mortality rate increased 16.8 times in patients with PE who had a CHA2DS2-VASc score above 4. The CHA2DS2-VAS score with cut-off value 2, with 71% sensitivity and 61% specificity, predicted mortality in this study. Like the CHA2DS2-VASc score, the ATRIA score is another scoring system that can be used to determine risk and prognosis for all diseases with thrombosis in their pathogenesis, especially cardiovascular diseases. Although the ATRIA score was

Table 1. Clinical and laboratory data of the study population

	PE group (n=198)	Non-PE group (n=280)	p-value
Age, years	64.4±16.8	63.6±9.7	0.142
Male, n (%)	103 (52)	172 (61.4)	0.040*
Hypertension, n (%)	85 (42.9)	87 (31)	0.079
Diabetes mellitus, n (%)	38 (19.1)	64 (22.8)	0.108
Coronary artery disease, n (%)	47 (23.7)	83 (29.6)	0.116
Heart failure, n (%)	9 (4.5)	20 (7.1)	0.234
Stroke, n (%)	2 (1)	8 (2.8)	0.146
Malignancy, n (%)	20 (10.1)	8 (2.8)	0.001*
History of operation, n (%)	22 (11.1)	10 (3.59)	0.001*
Deep vein thrombosis, n (%)	84 (42.4)	33 (11.7)	<0.001*
HG, g/dL	13.1±2.0	13.6±2.1	0.245
WBC, 10^3/µL	10.9±4.8	5.2±3.2	<0.001*
PLT, 10^3/µL	235.3±107.7	248.0±74.7	0.007*
Neutrophil, 10^3/µL	8.4±4.3	5.9±2.4	<0.001*
Lymphocyte, 10^3/µL	1.7±1.2	2.2±1.4	0.006*
D-dimer, µg/L	12187.0±1947.5	469.9±239.4	<0.001*
CRP, mg/L	80.3±7.1	5.9±2.4	<0.001*
Troponin, ng/L	326.6±113.2	24.8±15.1	0.001*
BNP, µg/L	948.6±120.1	85.3±28.5	<0.001*
ATRIA score	3.5±2.5	2.7±2.3	<0.001*
CHA2DS-VASc score	2.2±1.3	1.9±1.4	0.020*

PE: Pulmonary embolism, ATRIA: Anticoagulation and risk factors in atrial fibrillation, BNP: Brain natriuretic peptide, CHA2DS2-VASc: C: Congestive heart failure or left ventricular systolic dysfunction, H: Hypertension, A: Age of ≥75 years, D: Diabetes mellitus, S: Previous stroke, V: Vascular disease, A: Age between 65 and 74 years, Sc: Female gender, HG: Hemoglobin, PLT: Platelets, WBC: White blood cell count

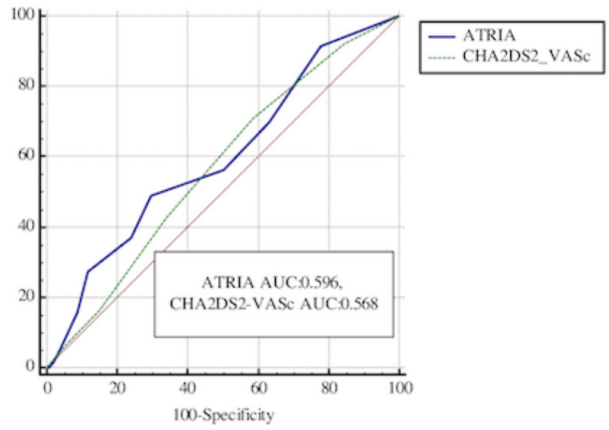

Figure 2. ROC curve analysis of ATRIA and CHA2DS2-VASc scores for predicting PE
ROC: Receiver operating characteristics, ATRIA: Anticoagulation and risk factors in atrial fibrillation, PE: Pulmonary embolism

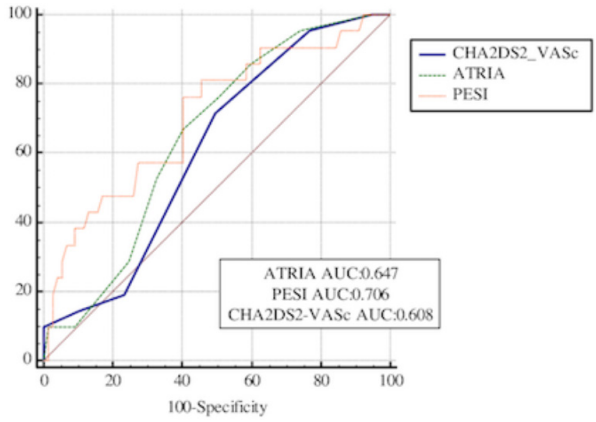

Figure 3. ROC curve analysis of PESI, ATRIA and CHA2DS2-VASc scores for predicting mortality in PE
ROC: Receiver operating characteristics, PE: Pulmonary embolism, PESI: Pulmonary embolism severity index, ATRIA: Anticoagulation and risk factors in atrial fibrillation

Table 2. Clinical and laboratory data of the PE group

	Mortality group (n=21)	Non-mortality group (n=177)	p-value
Age, years	73.7±12.1	63.3±16.9	0.007*
Male, n (%)	8 (38)	95 (54)	0.177
PE type, massive, n (%) Submassive, n (%) Non-massive, n (%)	5 (24) 6 (28) 10 (47)	3 (2) 20 (11) 154 (87)	<0.001*
Hypertension, n (%)	6 (28)	79 (45)	0.160
Diabetes mellitus, n (%)	4 (19)	34 (19)	0.986
Coronary artery disease, n (%)	5 (24)	42 (24)	0.993
Heart failure, n (%)	3 (14)	6 (3)	0.057
Stroke, n (%)	1 (5)	1 (1)	0.201
Malignancy, n (%)	20 (95)	0 (0)	<0.001*
History of operation, n (%)	21 (100)	1 (1)	<0.001*
Deep vein thrombosis, n (%)	21 (100)	63 (36)	<0.001*
HG, g/dL	11.2±2.8	11.6±1.9	0.405
WBC, 10^3/µL	11.4±4.0	10.8±4.9	0.580
PLT, 10^3/µL	263.9±138.6	231.9±103.3	0.199
Neutrophil, 10^3/µL	9.5±4.2	8.3±4.3	0.217
Lymphocyte, 10^3/µL	1.2±0.6	1.8±2.3	0.282
D-dimer, µg/L	12254.0±2014.5	11702.0±1443.8	0.927
CRP, mg/L	81.7±72.4	68.9±62.0	0.441
Troponin, ng/L	493.6±191.4	303.2±98.4	0.483
BNP, µg/L	1045.1±1374.3	940.3±1194.4	0.826
ATRIA score	5.2±2.1	3.3±2.4	0.001*
CHA2DS-VASc score	3.0±1.2	2.1±1.3	0.004*
PESI score	125.5±36.7	93.3±29.7	<0.001*

ATRIA: Anticoagulation and risk factors in atrial fibrillation, BNP: Brain natriuretic peptide, CHA2DS2-VASc: C: Congestive heart failure or left ventricular systolic dysfunction, H: Hypertension, A: Age of ≥75 years, D: Diabetes mellitus, S: Previous stroke, V: Vascular disease, A: Age between 65 and 74 years, Sc: Female gender, HG: Hemoglobin, PESI: Pulmonary embolism severity index, PLT: Platelets, WBC: White blood cell count

Table 3. Pairwise comparison of receiver operating characteristics (ROC) curves of ATRIA, CHA2DS2-VASc and PESI scores for mortality in patients with PE

	Difference between AUC	SE	95% CI	Z statistics	p-value
ATRIA-PESI	0.0588	0.0561	-0.0513-0.169	1.046	0.295
ATRIA-CHA2DS2-VASc	0.0393	0.0479	-0.0547-0.133	0.819	0.412
PESI-CHA2DS2-VASc	0.0980	0.0561	-0.0583-0.254	1.229	0.219

ATRIA: Anticoagulation and risk factors in atrial fibrillation, AUC: Area under curve, CHA2DS2-VASc: C: Congestive heart failure or left ventricular systolic dysfunction, H: Hypertension, A: Age of ≥75 years, D: Diabetes mellitus, S: Previous stroke, V: Vascular disease, A: Age between 65 and 74 years, Sc: Female gender, CI: Confidence interval, PESI: Pulmonary embolism severity index, SE: Standard error

emphasized in many studies evaluating the prognosis in myocardial infarction, no-reflow in STEMI, and end-points in HF, no study investigating the relationship between PE and the ATRIA score has yet been conducted (35-38). Our study is important in that it shows the ATRIA score is higher in patients with PE and can predict mortality. It was found in this study that both ATRIA and CHA2DS2-VASc scores were correlated with the PESI score, and all three scores in the ROC curve analysis had similar results in predicting mortality.

Study Limitations

The most important limitations of our study are that it was single-centered and the number of participants was low. Second, it was retrospective. Furthermore, we had no data about proteinuria. Since those with a known history of embolism were excluded, it is impossible to provide information on whether the scores used are predictive of PE recurrence or recurrence risk or prognosis. There is a need for multicenter, prospective studies with many participants in this regard. Despite these limitations, our study will contribute to the literature as it is the first study to evaluate the ATRIA score in PE and to compare the CHA2DS2-VASc and ATRIA scores with the PESI score in determining the risk of mortality.

Conclusion

The easily calculated and more widely used ATRIA and CHA2DS2-VASc scores can be used as an alternative to the PESI score in evaluating the diagnosis of PE and predicting mortality in PE compared to a scoring system such as the PESI score, which is complex and requires many parameters.

Ethics

Ethics Committee Approval: The study protocol was approved by the Adana City Training and Research Hospital Clinical Research Ethics Committee with the date 14.7.2021 and number 1492.

Informed Consent: Participants were included in the study after their consent was obtained.

Authorship Contributions

Concept: O.O.A., A.Y., Design: O.O.A., M.K., S.A., Data Collection and/or Processing: O.O.A., S.A., Analysis and/or Interpretation: O.O.A., A.Y., M.K., F.D., Literature Research: O.O.A., S.A., N.Y.K., F.D., M.D., Writing: O.O.A., S.A., A.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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