Relationship between CHA2DS2-VASc and CHADS2 scores with pulmonary hypertension in patients with acute pulmonary embolism

Abstract

Introduction: Pulmonary hypertension (PH) is the most important prognostic factor after acute pulmonary embolism (PE). Therefore, determination of patients who will develop PH after acute PE is crucial. The aim of the present study was to evaluate the predictive value of the CHADS2 and CHA2DS2-VASc scores for PH in patients with acute PE.

Material and methods: Seventy-nine adults who presented with acute PE, had an admission systolic pulmonary artery pressure (sPAP) measured on echocardiogram and no previous history of PE, were retrospectively identified from the computerized database. 31 patients who had sPAP ≤ 40 mm Hg were categorized as a “normal pulmonary pressure” group, whereas 48 patients who had sPAP > 40 mm Hg were categorized as a “PH” group.

Results: SPAP was > 40 mm Hg in 48 patients (60.8%), with a mean sPAP of 60.9 ± 16.1 mm Hg (median = 60, min–max = 41–100 mm Hg). In multivariate logistic regression models adjusted for CHADS2 and CHA2DS2-VASc score components, only age was found to be related with the development of PH. SPAP was weakly positively correlated with CHADS2 (p = 0.047; r = 0.224) and CHA2DS2-VASc (p = 0.023; r = 0.256) scores. SPAP values were increasing with the severity of the scores.

Conclusions: Both CHADS2 and CHA2DS2-VASc scores could be useful in the determination of which patients should be closely followed up in order to prevent the development of PH after acute PE.

Key words: CHA2DS2-VASc score, CHADS2 score, pulmonary hypertension, acute pulmonary embolism

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Introduction

Acute pulmonary embolism (PE) is one of the major causes of mortality, morbidity, and hospitalization worldwide [1]. Since patients older than 40 years are at an increased risk compared with younger patients, and the risk approximately doubles with each subsequent decade, an ever-larger number of patients are expected to be diagnosed with PE in the future [2]. The most important short- and long-term complication of PE is pulmonary hypertension (PH). The occurrence of PH after acute PE is strongly related with prognosis [3]. Hence, the risk stratification of PE to determine the development of PH is crucial.

The CHA2DS2-VASc (congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, previous stroke or transient ischemic attack (TIA), vascular disease, age 65 to 74 years, female gender) score and CHADS2 (congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, previous stroke or TIA) scores are used for embolic risk stratification in patients with atrial fibrillation (AF) [4]. Recent studies have demonstrated that both scores can predict prognosis in subjects with stable coronary artery disease, acute coronary syndrome and coronary artery bypass grafting surgery, irrespective of the presence of AF [5–7].

The aim of the present study is to evaluate the relation of CHA2DS2-VASc and CHADS2
scores with the development of PH in patients with acute PE.

**Material and methods**

In this retrospective study, 79 patients with diagnoses of PE were consecutively selected from hospital database. The patients’ demographic, laboratory and echocardiographic data were obtained from hospital records. The study was in compliance with the principles outlined in the Declaration of Helsinki and approved by the local ethics committee.

Diagnosis of PE was made by an emergency department physician, cardiologist and chest disease consultant. Thoracal pulmonary computed tomography angiography (CTA) was performed to all the patients. Admission symptoms, hemodynamic profile, electrocardiographic features and echocardiographic findings were obtained from hospital records. The patients’ clinical and demographic characteristics, encompassing age, gender, history of arterial hypertension, diabetes mellitus, tobacco use, left ventricular (LV) ejection fraction and systolic pulmonary arterial pressure measurement (sPAP) were noted.

The estimation of sPAP was calculated by the peak tricuspid regurgitation velocity (TRV) taking into account right atrial pressure (RAP) as described by the simplified Bernoulli equation [8]. RAP was estimated by echocardiography based on the diameter and respiratory variation in diameter of the inferior vena cava (IVC): an IVC diameter < 2.1 cm that collapses > 50% with a sniff suggested a normal RAP of 3 mm

| Table 1. Basic demographic, clinical, laboratory and echocardiographic features of the study population |
|--------------------------------------------------------|--------------------------------------------------------|-------------------------------|
| **Age** | Normal pulmonary pressure group | 60.2 ± 17.3 | Pulmonary hypertension group | 69.9 ± 14.2 | P | 74 (29–88) | 0.007* |
| **Male sex** | 18 | 58.10% | 25 | 52.10% | 0.602 |
| **Congestive heart failure** | 3 | 9.70% | 7 | 14.60% | 0.732 |
| **Diabetes** | 11 | 35.50% | 22 | 45.80% | 0.362 |
| **Hypertension** | 18 | 58.10% | 28 | 58.30% | 0.981 |
| **Coronary artery disease** | 17 | 54.80% | 17 | 35.40% | 0.089 |
| **Peripheral artery disease** | 2 | 6.50% | 5 | 10.40% | 0.698 |
| **Stroke or TIA history** | 1 | 3.20% | 9 | 18.80% | 0.079 |
| **Hiperlipidemi** | 10 | 32.30% | 13 | 27.10% | 0.621 |
| **Glucose (mg/dL)** | 109.6 ± 34.4 | 98.5 (62–196) | 116.6 ± 36.5 | 106 (69–215) | 0.27 |
| **Creatinine (mg/dL)** | 0.9 ± 0.2 | 0.9 (0.4–1.1) | 1.1 ± 0.5 | 0.9 (0.6–1.1) | 0.481 |
| **Uric acid (mg/dL)** | 5.5 ± 2 | 5.4 (2.2–9.2) | 7.7 ± 2.8 | 6.3 (4.6–15.7) | 0.01* |
| **Hemoglobin (g/dL)** | 12.5 ± 2 | 12.2 (8.7–15.8) | 13.7 ± 11.4 | 12.1 (7.1–88.9) | 0.418 |
| **Platelet count (10³/mL)** | 255.1 ± 84 | 250 (94–450) | 237 ± 89.6 | 232 (57–419) | 0.381 |
| **White blood cell count (10³/mL)** | 7.8 ± 2.3 | 7.5 (3.4–14.3) | 8.2 ± 2.9 | 7.6 (3.7–19) | 0.77 |
| **Troponin I (ng/mL)** | 1.3 ± 2.7 | 0.2 (0–8.7) | 0.5 ± 0.6 | 0.2 (0–2.7) | 0.797 |
| **CK-MB (mg/L)** | 24.9 ± 13.7 | 31 (0.2–40) | 28.1 ± 10.1 | 28 (0.3–48) | 0.969 |
| **D-dimer (mcg/L)** | 5.2 ± 4.7 | 4.4 (1–24.1) | 5.9 ± 5.6 | 4.3 (0–23) | 0.969 |
| **C reactive protein** | 36.9 ± 33.3 | 17.2 (4–96) | 34.6 ± 29.3 | 26.1 (0.1–132) | 0.728 |
| **LV ejection fraction (%)** | 55.9 ± 8 | 60 (30–66) | 50.3 ± 12.1 | 55 (20–65) | 0.008* |
| **SPAP (mm Hg)** | 34.3 ± 4.2 | 34 (28–40) | 60.9 ± 16.1 | 60 (41–100) | 0.0001* |
| **CHADS² score** | 1.3 ± 1.2 | 1 (0–5) | 2 ± 1.4 | 2 (0–5) | 0.024* |
| **CHADS²-VASc score** | 2.6 ± 1.9 | 2 (1–8) | 3.5 ± 1.9 | 3.5 (0–7) | 0.015* |

Data are presented as mean ± std deviation, median (min–max values) or number (percentage). *P < 0.05 statistically significant; Independent Samples T test; Mann-Whitney U test; Chi Square Test; CHADS²-VASc — congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease, age 65 to 74 years, female gender; CHADS² — congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke or transient ischemic attack; CK-MB — creatinine kinase myoglobin isofrom; DVT — deep venous thrombosis; LV — left ventricular; SPAP — systolic pulmonary artery pressure; TIA — transient ischemic attack.
Hg (range 0–5 mm Hg), whereas an IVC diameter > 2.1 cm that collapses < 50% with a sniff or on quiet inspiration suggested a high RAP of 15 mm Hg (range 10–20 mm Hg). In patients in whom the IVC diameter and collapse did not fit this paradigm, an intermediate value of 8 mm Hg (range 5–10 mm Hg) was used. PH was defined as an increase in mean pulmonary arterial pressure (mPAP) ≥ 25 mm Hg, and a sPAP of 40 mm Hg typically implies a mPAP more than 25 mm Hg [8].

On the basis of the CHA2DS2-VASc score, patients were assigned 1 point for congestive heart failure, hypertension, age 65–74 years, diabetes mellitus, vascular disease, female sex; 2 points for age 75 years or older and previous stroke or TIA. CHADS2 score was calculated by the sum of 1 point for each congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus and 2 points for previous stroke or TIA.

Data analysis was performed using SPSS Statistics for Windows, version 24.0 (SPSS, Inc., Chicago, IL, USA). Kolmogorov-Smirnov and Shapiro-Wilk tests were used to examine distribution pattern. Data were presented as mean ± standard deviation, median (minimum–maximum values) for continuous variables. The number of cases and percentages were used for categorical data. Independent Samples T test was applied for comparisons of data that were normally distributed; otherwise the Mann-Whitney U test was applied. Categorical data were analyzed using the Chi Square test. The effect of each different variable on the development of PH was calculated in univariate and multivariate analysis. Receiver operating characteristics (ROC) curve analysis was performed to find the best cut-off points of CHADS2 and CHA2DS2-VASc scores for the development of PH. P-value <0.05 was considered statistically significant.

### Results

A total of 79 patients (mean age: 66.1 ± 16.1 years, 54.4% men) were included in the study. Patients were grouped according to sPAP values on admission. Thirty-one patients who had sPAP ≤ 40 mm Hg were categorized as the “normal pulmonary pressure” group, whereas 48 patients (60.8%) who had sPAP > 40 mm Hg were categorized as the “PH” group.

Basic demographic, clinical and laboratory parameters of patients are presented in Table 1. SPAP value of the normal pulmonary pressure group was significantly lower than the pulmonary hypertension group (p < 0.0001). CHADS2 and CHA2DS2-VASc scores were significantly higher in the PH group (p = 0.024; p = 0.015). There was no significant difference in terms of PE risk factors, including malignancy, surgery, immobilization, pregnancy, deep venous thrombosis and travel history (Table 2).

According to univariate logistic regression analysis, CHADS2 score [odds ratio (OR): 1.538, 95% CI 1.043–2.268, p = 0.030], CHA2DS2-VASc score (OR: 1.318, 95% CI 1.016–1.711, p = 0.038), age (OR: 1.041, 95% CI 1.009–1.073, p = 0.012) and LV ejection fraction (OR: 0.939, 95% CI 0.885–0.997, p = 0.038) were found to be related to PH (Table 3).

In multivariate logistic regression models adjusted for CHADS2 and CHA2DS2-VASc score components, only age was found to be related with the development of PH (OR: 1.037, p = 0.030 in model 1; OR: 1.041, p = 0.024 in model 2).

ROC curve analysis for CHADS2 and CHA2DS2-VASc scores and PH were shown in Figure 1 and 2. The optimal cut-off value of CHADS2 and CHA2DS2-VASc scores for predicting the development of PH were 1.5 and 2.5, respectively in ROC curve analysis. Any CHADS2 value greater
than 1.5 had a sensitivity of 58%, a specificity of 58%, and any CHA2DS2-VASc score greater than 2.5 had a sensitivity of 60% and a specificity of 58% to predict the occurrence of PH.

There was a weak positive correlation between sPAP and CHADS2 (p = 0.047; r = 0.224) and CHA2DS2-VASc (p = 0.023; r = 0.256) scores (Figure 3–4). Increased sPAP values were associated with increased scores.

**Discussion**

Acute PE, which is an emergency condition, requires precise recognition and timely risk stratification, because early recognition and accurate risk stratification determine prognosis [8]. Risk stratification in acute PE begins with initial hemodynamic status assessment at an emergency department, being a well-established marker of prognosis. It is followed by laboratory tests and echocardiographic evaluation. Large and multiple emboli abruptly increase pulmonary vascular resistance and cause PH which in turn causes right ventricular (RV) strain. An acute increase of pulmonary pressure is directly related to RV

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**Table 3. Univariate and multivariate logistic regression analyses to predict pulmonary hypertension**

| Variable                                    | Odds ratio | 95% Confidence interval | P   |
|----------------------------------------------|------------|-------------------------|-----|
| Age                                          | 1.041      | 1.009–1.073             | 0.012 |
| Gender (male)                                | 1.274      | 0.512–3.167             | 0.602 |
| Coronary artery disease                      | 0.452      | 0.180–1.136             | 0.091 |
| Congestive heart failure                     | 1.593      | 0.379–6.694             | 0.525 |
| Hypertension                                 | 1.011      | 0.405–2.526             | 0.981 |
| Diabetes mellitus                            | 1.538      | 0.607–3.897             | 0.364 |
| Peripheral artery disease                    | 1.686      | 0.306–9.286             | 0.548 |
| D-dimer (mcg/L)                              | 1.027      | 0.915–1.152             | 0.656 |
| Chronic obstructive pulmonary disease        | 0.473      | 0.116–1.920             | 0.295 |
| LV ejection fraction (%)                     | 0.939      | 0.885–0.997             | 0.038 |
| CHADS2 score                                 | 1.538      | 1.043–2.268             | 0.030 |
| CHA2DS2-VASc score                           | 1.318      | 1.016–1.711             | 0.038 |

**Multivariate models**

**Model 1**

| Variable                                    | Odds ratio | 95% Confidence interval | P   |
|----------------------------------------------|------------|-------------------------|-----|
| Congestive heart failure                     | 1.041      | 0.219–4.959             | 0.959 |
| Hypertension                                 | 1.668      | 0.598–4.653             | 0.328 |
| Age                                          | 1.037      | 1.004–1.071             | 0.030 |
| Diabetes mellitus                            | 0.687      | 0.249–1.892             | 0.467 |
| Stroke history                               | 0.185      | 0.020–1.883             | 0.134 |

**Model 2**

| Variable                                    | Odds ratio | 95% Confidence interval | P   |
|----------------------------------------------|------------|-------------------------|-----|
| Congestive heart failure                     | 1.637      | 0.305–8.777             | 0.565 |
| Hypertension                                 | 1.455      | 0.494–4.280             | 0.496 |
| Age                                          | 1.041      | 1.005–1.078             | 0.024 |
| Diabetes mellitus                            | 0.780      | 0.259–2.349             | 0.659 |
| Stroke history                               | 0.125      | 0.019–1.624             | 0.125 |
| Coronary artery disease                      | 2.889      | 0.976–8.551             | 0.055 |
| Female sex                                   | 0.801      | 0.272–2.354             | 0.686 |

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![Figure 1](image1.png) **Figure 1.** Receiver operating characteristic curve analyses of CHADS2 score for pulmonary hypertension

![Figure 2](image2.png) **Figure 2.** Receiver operating characteristic curve analyses of CHA2DS2-VASc score for pulmonary hypertension
myocardial damage, and it is connected with prognosis [9]. Because of these reasons, estimation of pulmonary pressure by invasive or non-invasive techniques is important. In the acute setting of PE, invasive pulmonary pressure analysis is not an easy one, therefore, echocardiographic evaluation is the cornerstone of the prognosis assessment.

Over the past decade, it has been documented that sPAP may help estimate mPAP in adults with high accuracy and reasonably good precision [10]. The 25 mm Hg threshold used to define PH could correspond to an sPAP of 38–40 mm Hg [11]. Although the limits of the echocardiographic estimation of sPAP are widely appreciated, the results from invasive studies support an evidence-based sPAP-derived mPAP value, which is currently used to diagnose and follow patients with PH. As suggested by these researches, in this study, we determined the subjects with PH based on echocardiographic sPAP values over 40 mm Hg.

Chronic thromboembolic pulmonary hypertension (CTEPH) is a clinical entity with high pulmonary pressure that occurs after a thromboembolic event. More than 70% of CTEPH patients have an history of PE [12]. Therefore, individuals with PE should be screened routinely for the development of CTEPH.

CHADS2 and CHA2DS2-VASc scores are clinical thromboembolic risk scores for predicting stroke in patients from the high-risk population and with non-valvular AF [13]. However, recent studies have demonstrated that both scores can predict mortality in various cardiovascular diseases, irrespective of the presence of AF [14, 15]. In our study, the subjects with PH had significantly higher CHA2DS2-VASc and CHADS2 scores compared to the normal pulmonary pressure group. We found a positive correlation between sPAP and CHADS2 and CHA2DS2-VASc scores. Among CHA2DS2-VASc score components; age, hypertension, diabetes mellitus and the presence of vascular disease are well-known risk factors for deep venous thrombosis, which are also the risk factors for acute PE [16]. Therefore, these scores may be used to predict the development of PE and PH.

Although there was a significant difference in CHADS2 and CHA2DS2-VASc scores between patients with PH and normal pulmonary pressure groups, only older age reached statistical significance in multivariate regression analysis. This result showed us that the older age is the strongest predictor of PH after acute PE. Older age, especially above 80, is also one of the parameters of Pulmonary Embolism Severity Index (PESI), which is the most reliable and validated risk score system after acute PE [17]. The presence of chronic heart failure is also a parameter of CHADS2 and CHA2DS2-VASc scores, and it is also a component of a PESI index. The most recent 2019 European Society of Cardiology guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society recommends the determination of a clinical risk profile by using PESI index [17]. According to our current knowledge, our research is the first study using CHADS2 and CHA2DS2-VASc scores for risk stratification after acute PE.

On the other hand, the study has some limitations. First, it has a retrospective cross-sectional design with data from a single center. Due to the retrospective nature of our data and the small sample size, our findings can not be generalized...
to all populations. Second, pulmonary pressure estimation and determination of patients with PH were done with echocardiography. Invasive right heart catheterization was not performed. Finally, sPAP measurements were used instead of mPAP, which might have led to misdiagnosis of PH.

**Conclusions**

In our study, older age is the most important factor related to the development of PH after acute PE. Both CHADS2 and CHA2DS2-VASc scores could be useful in acute PE setting in the determination of which patients should be closely followed up so that more prolonged anticoagulation therapy and surveillance concerning the development of PH may be applied.

**Conflict of interest**

The authors declare no conflict of interest.

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