Predictive Value of CHA2DS2-VASc Stroke Risk Score for Major Adverse Cardiovascular Events in Patients with Three-Vessel or Left Main Coronary Artery Disease: Postprint

Authors: Wang Qiushi, Hongwei Li, Li Hongwei

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Abstract

Background: The SYNTAX score is one of the most commonly used scoring systems for predicting prognosis in patients with coronary artery disease based on coronary anatomy and lesion characteristics, and there is a clinical need for an assessment method based on general clinical data to enhance its predictive efficacy.

Objective: To investigate the relationship between the CHA2DS2-VASc stroke risk score and major adverse cardiovascular events (MACEs) in patients with coronary artery disease and triple-vessel disease (TVD) or left main disease (LMD).

Methods: This study included 630 TVD/LMD patients who underwent PCI treatment at Beijing Friendship Hospital, Capital Medical University between January 2009 and May 2014. Patients were divided into mild lesion group (0-22 points, n=276), moderate lesion group (23-32 points, n=249), and severe lesion group ($ $33 points, n=105) based on SYNTAX score. Pearson correlation analysis and partial correlation analysis were used to explore correlations between quantitative data, while univariate and multivariate Logistic regression analyses were employed to investigate whether CHA2DS2-VASc and SYNTAX scores were risk factors for MACE within 3 years. Receiver operating characteristic (ROC) curves were constructed to evaluate the efficacy of CHA2DS2-VASc score in predicting MACE within 3 years. The Delong method was used to compare ROC curves for CHA2DS2-VASc score, SYNTAX score, and the combination of both scoring systems in predicting MACE.

Results: There were statistically significant differences among different SYNTAX score groups in age, congestive heart failure, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), SYNTAX score,

CHA2DS2-VASc score, MACE within 3 years, death, and non-fatal myocardial infarction (P<0.05). The CHA2DS2-VASc score was significantly positively correlated with SYNTAX score (r=0.109, P=0.003). Multivariate Logistic regression analysis showed that hypertension [OR=1.753, 95%CI (1.047, 2.938)], LVEF [OR=0.962, 95%CI (0.942, 0.982)], SYNTAX score [OR=1.028, 95%CI (1.002, 1.055)], and CHA2DS2-VASc score [OR=1.210, 95%CI (1.070, 1.369)] were independent influencing factors for MACE (P<0.05). ROC curve analysis revealed that the area under the ROC curve (AUC) for SYNTAX score in predicting MACE was 0.638, and the AUC for CHA2DS2-VASc score was 0.619. The AUC for combined use of SYNTAX and CHA2DS2-VASc scores in predicting MACE was 0.685. Head-to-head comparison using the Delong method showed that the difference in AUC between SYNTAX and CHA2DS2-VASc scores for predicting MACE was 0.019 (P=0.587), indicating that both SYNTAX and CHA2DS2-VASc scores had predictive value for MACE, but the difference in AUC was not statistically significant. The difference in AUC between combined SYNTAX and CHA2DS2-VASc scores versus SYNTAX score alone in predicting MACE was 0.0469 (P=0.046), and versus CHA2DS2-VASc score alone was 0.0659 (P=0.043), both differences being statistically significant.

Conclusion: The CHA2DS2-VASc scoring system can be used to predict the severity of coronary artery lesions and the occurrence of MACE within 3 years in TVD/LMD patients, and combining CHA2DS2-VASc with SYNTAX scoring systems can effectively improve the predictive value for 3-year MACE.

Full Text

The Predictive Value of CHA_2DS_2-VASc Stroke Risk Score for Major Adverse Cardiovascular Events in Patients with Coronary Heart Disease and Three-Vessel or Left Main Disease

WANG Qiushi, LI Hongwei*

Department of Cardiology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China

Corresponding author: LI Hongwei, Chief physician; E-mail: lhw19656@sina.com

Abstract

Background: The SYNTAX score is one of the most commonly used scoring systems for predicting prognosis in patients with coronary heart disease (CHD) based on coronary anatomy and lesion characteristics. However, there is a clinical need for an evaluation method based on general clinical data to enhance its predictive efficacy.

Objective: To investigate the relationship between CHA_2DS_2-VASc stroke risk

scores and major adverse cardiovascular events (MACEs) in patients with three-vessel disease (TVD) or left main disease (LMD).

Methods: This study enrolled 630 TVD/LMD patients who underwent percutaneous coronary intervention (PCI) at Beijing Friendship Hospital, Capital Medical University between January 2009 and May 2014. Patients were stratified into three groups based on SYNTAX scores: mild lesion group (0–22 points, n=276), moderate lesion group (23–32 points, n=249), and severe lesion group ($ 33 points, n = 105). Pearson correlation and partial correlation analyses were used to explore relationships between year MACE. The Delong method was used to compare ROC curves for CHA{2}DS{2}$-VASc score, SYNTAX score, and the combined scoring system for MACE prediction.

Results: Significant differences were observed among the SYNTAX score groups in age, congestive heart failure, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), SYNTAX score, CHA_2DS_2-VASc score, 3-year MACE, death, and non-fatal myocardial infarction (P<0.05). CHA_2DS_2-VASc score showed a significant positive correlation with SYNTAX score (r=0.109, P=0.003). Multivariate logistic regression analysis identified hypertension [OR=1.753, 95%CI (1.047, 2.938)], LVEF [OR=0.962, 95%CI (0.942, 0.982)], SYNTAX score [OR=1.028, 95%CI (1.002, 1.055)], and CHA_2DS_2-VASc score [OR=1.210, 95%CI (1.070, 1.369)] as independent predictors of MACE (P<0.05). ROC analysis revealed an area under the curve (AUC) of 0.638 for SYNTAX score, 0.619 for CHA_2DS_2-VASc score, and 0.685 for the combined scoring system. Head-to-head comparison using the Delong method showed an AUC difference of 0.019 between SYNTAX and CHA_2DS_2-VASc scores (P=0.587), indicating both had predictive value for MACE but the difference was not statistically significant. The AUC difference between the combined score and SYNTAX score alone was 0.0469 (P=0.046), and between the combined score and CHA_2DS_2-VASc score alone was 0.0659 (P=0.043), both statistically significant.

Conclusion: The CHA_2DS_2-VASc scoring system can predict both coronary lesion severity and 3-year MACE occurrence in TVD/LMD patients. Combining CHA_2DS_2-VASc with SYNTAX scores effectively improves the predictive value for 3-year MACE.

Keywords: coronary artery disease; CHA_2DS_2-VASc score; SYNTAX score; triple-vessel disease; left main disease; predictive value

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Introduction

Coronary artery disease (CAD) remains one of the leading causes of death worldwide. Established risk factors for CAD include hypertension, smoking, hyperlipidemia, and diabetes, which can be addressed through lifestyle interventions and pharmacotherapy. Three-vessel disease (TVD) and left main disease (LMD) are

recognized as independent predictors of adverse clinical outcomes in CAD, with diagnosis and treatment dependent on invasive coronary angiography (CAG). The choice of therapeutic approach is determined by the severity of coronary lesions observed on CAG. The SYNTAX score, calculated based on coronary lesion characteristics, is a widely used risk stratification tool for CAD. Clinical guidelines both domestically and internationally recommend coronary artery bypass grafting (CABG) for patients with SYNTAX scores >32 and percutaneous coronary intervention (PCI) for those with scores <23. Previous studies have demonstrated that SYNTAX score correlates directly with mortality in CAD patients. However, the SYNTAX scoring system has limitations: it relies on CAG results, incorporates only imaging features of coronary lesions, and overlooks clinical comorbidities and other risk factors. Therefore, prospective risk stratification is crucial for pre-CAG assessment, prognostic evaluation, and clinical decision-making.

The CHA_2DS_2-VASc stroke risk score is primarily used for stroke risk stratification in patients with non-valvular atrial fibrillation and to guide anticoagulation therapy. The score incorporates age, sex, hypertension, diabetes, congestive heart failure, stroke, and peripheral vascular disease—all of which are also risk factors for atherosclerosis. Studies have confirmed that CHA_2DS_2-VASc score correlates with coronary lesion complexity and can predict MACE in CAD patients. Based on this evidence, we hypothesized that the CHA_2DS_2-VASc stroke risk score could predict both coronary lesion severity and MACE in CAD patients with TVD/LMD.

Methods

Study Population This retrospective study included 630 TVD/LMD patients who underwent PCI at Beijing Friendship Hospital, Capital Medical University between January 2009 and May 2014. Patients were stratified into three groups based on SYNTAX scores: mild lesion group (0–22 points, n=276), moderate lesion group (23–32 points, n=249), and severe lesion group ($ $33 points, n=105).

Inclusion Criteria: Patients aged >18 years who underwent CAG and PCI for CAD, with TVD/LMD confirmed by CAG. Coronary lesions were defined as $ $50% stenosis by visual estimation in native coronary vessels with diameter $ $1.5 mm. TVD was defined as lesions in the left anterior descending, left circumflex, and right coronary arteries. LMD was defined as left main coronary artery involvement.

Exclusion Criteria: Missing clinical data, severe anemia or active bleeding, chronic liver dysfunction, chronic kidney disease (CKD) stages 3–5, patients on regular dialysis, malignancy, severe aortic stenosis or regurgitation, or prior PCI/CABG history. The study protocol was approved by the Ethics Committee of Beijing Friendship Hospital, Capital Medical University (approval number:

2023-P2-113-01).

Data Collection General clinical data included age, sex, height, weight, smoking status, and comorbidities (hypertension, diabetes, congestive heart failure, peripheral vascular disease, atrial fibrillation, and stroke history). Laboratory results comprised complete blood count, blood biochemistry, echocardiography, and coronary angiography imaging data. Key parameters included hemoglobin, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum creatinine, and LVEF.

Clinical Endpoints Patients or their families were contacted by telephone to determine survival status within three years post-PCI and to identify events including cardiac death, all-cause death, non-fatal myocardial infarction, repeat revascularization, and rehospitalization for heart failure. MACE was defined as all-cause death and recurrent non-fatal myocardial infarction. Myocardial infarction was defined according to the Fourth Universal Definition of Myocardial Infarction, requiring evidence of acute myocardial injury (rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile upper reference limit) plus clinical evidence of acute myocardial ischemia.

Risk Factor Scoring **CHA_2DS_2-VASc Score:** Congestive heart failure (C), hypertension (H), diabetes (D), vascular disease (V), age 65–74 years (A), and female sex (Sc) each received 1 point; age $ $75 years (A2) and prior stroke/transient ischemic attack (S2) received 2 points, for a total possible score of 0–9.

SYNTAX Score: Two interventional cardiologists with associate senior professional titles or higher independently calculated SYNTAX scores by entering lesion characteristics into the official website (https://syntaxscore.org). In case of disagreement, a third senior interventional cardiologist adjudicated the score. The intraclass correlation coefficient (ICC) was 0.999 (P<0.001). eGFR was calculated using the simplified Modification of Diet in Renal Disease (MDRD) formula for Chinese patients: eGFR = $186 \times [\text{creatinine (mg/dl)}]^{-1 \cdot 154} \times [\text{age (years)}]^{-0 \cdot 203} \times (0.742$ for females).

Statistical Analysis Statistical analysis was performed using SPSS 26.0. Normality was assessed using the Kolmogorov-Smirnov test combined with histograms and Q-Q plots. Categorical variables were expressed as frequencies and percentages. Normally distributed continuous variables were expressed as mean ± standard deviation ($\bar{x}\pm s$), while non-normally distributed continuous variables were expressed as median (P25, P75). Categorical variables were compared using Pearson ^{2} test, normally distributed continuous variables using ANOVA, and non-normally distributed continuous variables using Kruskal-Wallis H test. Pearson and partial correlation analyses examined relationships between quantitative variables. Univariate and multivariate logistic regression analyses identified risk factors for 3-year MACE. Fine & Gray models analyzed competing

risks in MACE multiple outcomes. ROC curves evaluated the predictive efficacy of CHA_2DS_2-VASc score for 3-year MACE. The Delong method compared ROC curves between CHA_2DS_2-VASc score, SYNTAX score, and combined scoring system. Statistical significance was defined as $P<0.05$.

Results

Baseline Characteristics and Score Comparisons The study included 630 TVD/LMD patients: 9 with isolated LMD, 524 with isolated TVD, and 97 with both LMD and TVD. According to SYNTAX scores, 276 patients (43.81%) were in the mild lesion group, 249 (39.52%) in the moderate lesion group, and 105 (16.67%) in the severe lesion group. Significant differences among groups were observed in age, congestive heart failure, eGFR, LVEF, SYNTAX score, CHA_2DS_2-VASc score, 3-year MACE, death, and non-fatal myocardial infarction ($P<0.05$) .

Correlation Between CHA_2DS_2-VASc Score and Coronary Stenosis Severity Pearson correlation analysis revealed a significant positive correlation between CHA_2DS_2-VASc score and SYNTAX score ($r=0.263$, $P<0.001$). After adjusting for age, eGFR, LVEF, and congestive heart failure, partial correlation analysis confirmed that CHA_2DS_2-VASc score remained significantly positively correlated with SYNTAX score ($r=0.109$, $P=0.003$).

Correlation Between CHA_2DS_2-VASc Score and MACE During 3-year follow-up, 107 patients (17.0%) experienced MACE, including 73 all-cause deaths (11.6%) and 23 non-fatal myocardial infarctions (3.7%). MACE rates were 9.4% in the mild lesion group, 21.7% in the moderate lesion group, and 25.7% in the severe lesion group.

Univariate logistic regression analysis with MACE occurrence as the dependent variable (1=yes, 0=no) and covariates including sex, age, BMI, hypertension, diabetes, smoking, eGFR, LVEF, CHA_2DS_2-VASc score, and SYNTAX score showed that age, CHA_2DS_2-VASc score, and SYNTAX score were risk factors for MACE, while eGFR and LVEF were protective factors .

To avoid omitting important variables, multivariate logistic regression was performed on variables with $P<0.2$ in univariate analysis. Results showed that hypertension [OR=1.753, 95%CI (1.047, 2.938)], LVEF [OR=0.962, 95%CI (0.942, 0.982)], SYNTAX score [OR=1.028, 95%CI (1.002, 1.055)], and CHA_2DS_2-VASc score [OR=1.210, 95%CI (1.070, 1.369)] were independent risk factors for MACE .

Fine & Gray competing risk analysis revealed that SYNTAX score was a risk factor for all-cause death but not for non-fatal myocardial infarction, whereas CHA_2DS_2-VASc score was a risk factor for both all-cause death and non-fatal myocardial infarction .

Predictive Value of SYNTAX and CHA_2DS_2-VASc Scores for MACE
ROC analysis showed an AUC of 0.638 for SYNTAX score (optimal cutoff 23.5, sensitivity 75.0%, specificity 53.5%) and 0.619 for CHA_2DS_2-VASc score (optimal cutoff 3.5, sensitivity 67.3%, specificity 51.8%). The combined scoring system achieved an AUC of 0.685 (sensitivity 86.7%, specificity 56.3%) [Figure 1: see original paper].

Using the Delong method for head-to-head comparison, the AUC difference between SYNTAX and CHA_2DS_2-VASc scores was 0.019 (P=0.587), indicating both scores had predictive value for MACE but the difference was not statistically significant. The AUC difference between the combined score and SYNTAX score alone was 0.0469 (P=0.046), and between the combined score and CHA_2DS_2-VASc score alone was 0.0659 (P=0.043), both statistically significant .

Discussion

This retrospective analysis of 630 TVD/LMD patients demonstrated that CHA_2DS_2-VASc score can predict 3-year MACE occurrence in CAD patients with TVD/LMD. Combining CHA_2DS_2-VASc with SYNTAX scores improved sensitivity and specificity for MACE prediction, providing a more effective tool for identifying high-risk patients.

The SYNTAX scoring system is the most widely used tool for guiding coronary revascularization strategy. Our findings confirm that elevated SYNTAX scores correlate significantly with MACE in TVD/LMD populations, with 3-year MACE rates increasing from 9.4% in the mild lesion group to 25.7% in the severe lesion group. The SYNTAX trial reported similar trends: 19.4% in mild, 22.8% in moderate, and 28.2% in severe lesion groups. However, SYNTAX has limitations. First, it considers only anatomical features while ignoring clinical risk factors such as age, sex, and comorbidities. Previous studies have attempted to combine different scoring systems to incorporate these factors. Second, our Fine & Gray analysis showed SYNTAX predicts all-cause death but not non-fatal myocardial infarction, consistent with other TVD/LMD studies demonstrating its utility for predicting cardiac death and MACE but limited value for non-fatal MI. Conversely, CHA_2DS_2-VASc score predicted both outcomes.

Originally developed for stroke risk stratification in non-valvular atrial fibrillation, CHA_2DS_2-VASc has shown broader clinical utility. Large-scale studies in non-atrial fibrillation populations have demonstrated its ability to predict stroke, and coronary CTA studies have shown correlation with coronary stenosis severity. Our study confirms that CHA_2DS_2-VASc score independently correlates with coronary lesion severity in TVD/LMD patients. While the underlying pathophysiology remains unclear, all CHA_2DS_2-VASc components may participate in CAD development and progression. Most CAD patients have at least one coronary risk factor, which further increases risk. Previous studies have

shown CHA_2DS_2-VASc predicts all-cause mortality and MACE in CABG patients. Our findings validate that combining CHA_2DS_2-VASc with other clinical indicators can preliminarily predict coronary stenosis severity. ROC analysis showed CHA_2DS_2-VASc had 67.3% sensitivity and 51.8% specificity for MACE prediction, with the combined scoring system improving both parameters.

Study Limitations: (1) This single-center retrospective study requires cautious interpretation. (2) Significant renal function differences among groups may limit generalizability, though renal function was not a risk factor for MACE prediction, possibly due to exclusion of severe renal insufficiency. (3) Significant heart function differences existed, as heart failure is both a risk factor and consequence of MACE; larger prospective studies are needed. (4) The cohort included only post-PCI patients, excluding medical therapy or CABG patients, so conclusions cannot guide optimal revascularization strategy selection.

In conclusion, CHA_2DS_2-VASc score can predict MACE in CAD patients with TVD/LMD. The scoring system is simple, low-cost, and widely applicable, serving as a valuable supplement to SYNTAX for early identification of high-risk TVD/LMD patients.

Author Contributions: WANG Qiushi conceptualized and designed the study, collected and analyzed data, performed statistical analysis, created figures and tables, and drafted the manuscript. LI Hongwei supervised quality control and review and took overall responsibility for the manuscript. All authors approved the final version.

Conflict of Interest: None declared.

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Note: Figure translations are in progress. See original paper for figures.