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Original Research

The Role of Preoperative CHA2DS2-VASc Score in Predicting Late Saphenous Vein Graft Failure in Non-STEMI Patients with Prior Coronary Artery Bypass Grafting: A Retrospective Study

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Abstract

Objectives: Despite the prevalence of saphenous vein graft (SVG) failure following coronary artery bypass graft (CABG) surgery, SVGs continue to be widely used. This study aimed to investigate the value of the CHA2DS2-VASc score, originally developed for predicting thromboembolic events in atrial fibrillation, in predicting SVG failure post-CABG.

Methods: This retrospective study analyzed data from 526 patients with a history of CABG who presented with non-ST-elevation myocardial infarction between January 2017 and April 2024. SVG failure was defined as exhibiting stenosis of 70% or greater, or complete occlusion. Preoperative CHA2DS2-VASc scores were calculated for each patient. Multivariable analysis was conducted to identify independent predictors of SVG failure.

Results: Among the 526 patients, 242 (46%) experienced SVG failure. Patients with SVG failure exhibited higher CHA2DS2-VASc scores. Multivariable analysis identified the CHA2DS2-VASc score (OR: 2.203, 95% CI: 1.672-2.902, p<0.001), time interval after CABG (OR: 1.167, 95% CI: 1.081-1.259, p<0.001), and number of SVGs (OR: 2.378, 95% CI: 1.745-3.241, p<0.001) as independent predictors of SVG failure. Of those parameters, the CHA2DS2-VASc score demonstrated a higher AUC value (AUC=0.796, AUC=0.724, AUC=0.641, respectively).

Conclusion: Pre-operative CHA2DS2-VASc score may be predictive of late SVG failure after CABG.

Keywords: Cha2ds2-vasc score, coronary angiography, coronary artery bypass grafting, non-st elevation myocardial infarction, saphenous vein graft failure

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In the treatment with patients of coronary artery disease (CAD), coronary artery bypass grafting (CABG) remains essential despite improvements in percutaneous coronary intervention (PCI).[1,2] Regardless of the presence of diabetes mellitus (DM), the current European guidelines prefer CABG over PCI in a number of coronary syndromes, including left main disease and three-vessel CAD with an intermediate to high SYNTAX score (Level 1, Class A).[3,4] The great saphenous vein is still often used in CABG because of its length and accessibility, even though arterial conduits—particu-

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larly the left internal mammary artery (LIMA)—have shown better and more resilient graft results than the saphenous vein graft (SVG).[5] Worldwide, up to 95% of patients have CABG with at least one SVG in addition to the LIMA.[6] The reported patency rates for SVGs vary widely: 11-41% failure within less than 3 years, 19-33% failure within 5 to 10 years, and 39-61% failure at follow-ups exceeding 10 years.[5] SVGs are prone to progressive degeneration over time, displaying accelerated atherosclerosis even if they maintain patency. SVGs develop neointimal hyperplasia and foamy macrophages during the first year following anastomosis to the arterial system, which leads to stenotic lesions with enlarging necrotic cores.[7] This results in a high incidence of ischemia-driven events, distal embolization, and occlusive pathology. Therefore, it seems important to identify factors that contribute to graft failure in patients treated with SVG and to identify factors that predict graft failure.

A simple risk assessment method for determining the chance of stroke or thromboembolic events in people with non-valvular atrial fibrillation (AF) is the CHA2DS2-VASc score. This score method considers a number of variables, such as gender, age, diabetes mellitus, vascular disease, congestive heart failure (HF), hypertension (HT), and previous stroke history.[8] According to recent research, the CHA2DS2-VASc score may be used to forecast the severity and outcome of acute coronary syndrome.[9,10] Additionally, a study found that in patients receiving elective PCI with a drug-eluting stent, the CHA2DS2-VASc score was linked to de-novo coronary stenosis.[11] However, there are limited studies regarding the ability of this scoring system to predict SV failure in patients undergoing CABG. In order to evaluate the association between preoperative CHA2DS2-VASc score and SVG failure in patients undergoing CABG, we carried out a retrospective analysis.

Methods

Study Design and Population

Patients with a history of CABG who underwent coronary angiography after being diagnosed with non-ST-elevation myocardial infarction (NSTEMI) at a tertiary healthcare facility between January 2017 and April 2024 were included in this retrospective single-center analysis. Following the application of inclusion and exclusion criteria, 526 of the 785 patients who were initially under consideration were added to the study. The study cohort was stratified into two subgroups (SVG failure group and SVG patency group) based on the presence of atherosclerotic SVG failure, confirmed by angiography. Patients with a history of CABG with full arterial conduits, patients within the first year following CABG, patients for whom the preoperative CHA2DS2-VASc score could not be determined due to insufficient data, and patients with severe comorbidities such as advanced lung and kidney disease or cancers that were expected to cause death during the 6-month follow-up period were all excluded.

This study was approved by the Kartal Kosuyolu Research and Education Hospital Clinical Research Ethics Committee and followed the Declaration of Helsinki's guidelines. Participants' formal informed permission was acquired.

Data Collection and Determination of the CHA2DS2-VASc Score

Clinical characteristics and laboratory parameters of the patients before CABG were retrieved from the hospital's electronic health records and national database. Demographic information including age and gender, as well as data on HT, hyperlipidemia, and DM, HF, and stroke or transient ischemic attack (TIA) history were obtained. Lastly, each patient's pre-operative CHA2DS2-VASc score was calculated, with 1 point awarded for HT, DM, and HF, and 2 points for age ≥ 75 years and a history of stroke or TIA.[8]

Coronary Angiographic Evaluation

Coronary angiography was performed via the femoral artery. Intravenous heparin was administered to all patients in accordance with current guidelines.[3] Selective injections were administered to the LIMA and each aortic anastomosis. An aortic root angiography was performed in situations where graft or stump injection was unable to determine the SVG's condition. Diverse projections were employed to ensure comprehensive coverage of arterial grafts, coronary arteries, and SVGs, enabling subsequent quantitative analysis. Two experienced cardiologists independently evaluated SVG patency by meticulously analyzing coronary angiographic images. A graft was classified as failed if it exhibited stenosis of 70% or greater, or if it was entirely occluded. On the other hand, if a graft displayed less than 70% stenosis and the complete graft course could be seen, it was deemed patent.[12]

Statistical Analysis

While categorical data were presented as absolute and percentage values, continuous research data were presented as mean and standard deviation values. Pearson's chi-squared or Fisher's exact test was used to compare categorical data groups, while the independent samples t-test and Mann-Whitney U test were used to compare independent continuous data groups. The independent predictors of the dependent variable (SVG failure) were identified using crude univariate and adjusted multivariable regression analysis. The odds ratio (OR) was used to describe the

model's coefficients, and 95% was the confidence interval (CI). Based on identifying the ideal cutoff value for SVG failure predictions, the receiver operating characteristic (ROC) curve analysis was utilized to elucidate the connections between the factors under consideration and SVG failure. Statistical significance was defined as 2-tailed probability (p) values less than 0.05 for all statistical analyses. Jamovi and R 4.01 software (Vienna, Austria) with the "ggplot," "Hmisc," and "rms" packages were used for all statistical analyses.

Results

The study population consisted of 526 patients, with 242 (46%) patients with SVG failure versus 284 (54%) patients with SVG patency. Based on SVG failure, Table 1 displayed the research population's demographic and clinical characteristics. In the SVG failure group, the proportion of male patients was considerably lower than in the SVG patency group (73.1% vs. 82.4%, p=0.01). HT, DM, CKD, cerebrovascular disease and AF were more common in patients with SVG failure than patients with SVG patency (p<0.001, p<0.001, p<0.001, p=0.005, p=0.024, respectively). In addition, patients with SVG failure had substantially higher CHA2DS2-VASc scores, the number of SVGs, and the time interval following CABG than patients with SVG patency (p<0.001, for all). Furthermore, patients with SVG failure had lower ejection fractions (EF) and statin usage in contrast to another group (p<0.001, p=0.017, respectively). A box plot demonstrating the distribution of CHA2DS2-VASc values in patients with SVG failure and with SVG patency was presented in Figure 1. Table 2 presents comparisons of relevant laboratory parameters based on the SVG failure. White blood cell and hemoglobin levels were significantly lower among the patients with SVG failure (p=0.03, p=0.031, respectively). However, those with SVG failure had noticeably greater triglyceride levels (p=0.031).

The predictors associated with the risk of SVG failure were determined through a multivariable logistic regression analysis, as outlined in Table 3. The selection of covariates is based on clinical judgement, comorbidities, and statistically significant variables in univariable analysis. This model

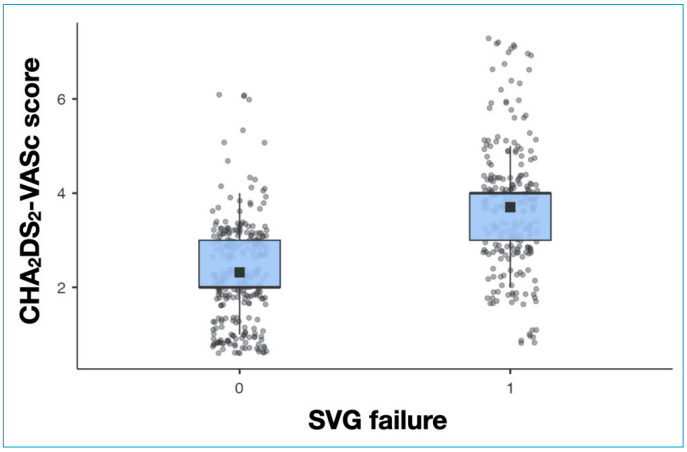

Figure 1. Box plot demonstrating the distribution of CHA2DS2-VASc values in patients with SVG failure and with SVG patency.

Table 1. Demographic and clinical characteristics of study patients based on SVG failure

Variables	Patients with SVG failure n=242 (46%)	Patients with SVG patency n=284 (54.0%)	p
Age (years)	67±9.24	65.5±8.74	0.061
Gender (male), n (%)	177 (73.1)	234 (82.4)	**0.01**
HT, n (%)	220 (91.7)	210 (73.9)	**<0.001**
DM, n (%)	128 (52.9)	92 (32.4)	**<0.001**
CKD, n (%)	56 (23.1)	34 (12)	**<0.001**
Cerebrovascular Disease, n (%)	28 (11.6)	14 (4.9)	**0.005**
EF (%)	55 (40-65)	55 (55-65)	**<0.001**
Atriyal fibrillation, n (%)	29 (12)	18 (6.3)	**0.024**
CHA2DS2-VASc score	4 (3-4)	2 (2-3)	**<0.001**
Time interval after CABG (year)	7 (5-9)	4 (2-6)	**<0.001**
The number of SVGs	3 (2-3)	2 (2-3)	**<0.001**
Beta-blocker usage, n (%)	228 (94.2)	266 (94.3)	0.956
ACEi usage, n (%)	158 (65.8)	181 (63.7)	0.616
Oral anti-diabetic usage, n (%)	61 (25.6)	62 (21.8)	0.308
Insulin usage, n (%)	25 (10.4)	19 (6.7)	0.125
Statin usage, n (%)	168 (69.4)	223 (78.5)	**0.017**

ACEi: angiotensin converting enzyme inhibitors; CABG: coronary artery bypass grafting surgery; SVGs: saphenous vein grafts; HT: hypertension; DM: diabetes mellitus; CKD: chronic kidney disease; EF: ejection fraction.

Table 2. Comparison of laboratory findings of the groups based on SVG failure

Variables	Patients with SVG failure n=218 (44%)	Patients with SVG patency n=278 (56.0%)	p
WBC (10^3/μL)	7.75 (5.80-10.37)	8.90 (6.60-10.20)	**0.03**
Hemoglobin (g/dL)	13.50 (12.20-14.20)	13.65 (12.60-14.80)	**0.031**
Platelet (10^3/μL)	240 (193-267)	227.5 (188-280)	0.823
Total Cholesterol (mg/dL)	184.2 (158.8-210.8)	189 (157.75-214.60)	0.869
Triglyceride (mg/dL)	158 (131.25-217)	145 (114-237)	**0.031**
HDL-C (mg/dL)	41 (38-44)	41 (37-49)	0.490
LDL-C (mg/dL)	107 (85-135)	108 (82-138)	0.989
eGFR (ml/min/1.73 m^2)	71.1 (38.3-105)	77 (65.8-88.2)	0.089
Creatinine (mg/dL)	1.05 (0.75-1.63)	0.98 (0.88-1.16)	0.185
Uric acid (mg/dL)	5.8 (5.4-6.7)	5.7 (5.4-6.5)	0.856
CRP (mg/L)	10 (4-35.5)	9.5 (3-40)	0.288
Albumin (g/dL)	4.0 (3.80-4.10)	3.9 (3.60-4.30)	0.413

CRP: C reactive protein; eGFR: estimated glomerular filtration rate; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein; WBC: white blood cell; SVG: saphenous vein graft.

Table 3. Multivariable analysis for prediction of SVG failure

Variables	Multivariable analysis			
	p	OR	95% Confidence Interval (CI)	
			Lower	Upper
Age (years)	0.072	0.974	0.947	1.002
Gender (male)	0.165	1.550	0.835	2.876
CHA2DS2-VASc score	**<0.001**	2.203	1.672	2.902
Time interval after CABG (year)	**<0.001**	1.167	1.081	1.259
The number of SVGs	**<0.001**	2.378	1.745	3.241
CKD	0.530	1.258	0.615	2.572
Statin usage	**0.003**	0.432	0.248	0.751
EF (%)	0.263	0.986	0.961	1.011
Atrial fibrillation	0.125	0.516	0.221	1.201
Hemoglobin	0.142	0.883	0.748	1.042

CKD: chronic kidney disease; CABG: coronary artery bypass grafting surgery; SVG: saphenous vein graft; CRP; EF, ejection fraction; OR: odds ratio; CI: confidence interval.

included covariates such as age, gender (male), CHA2DS2-VASc score, time interval after CABG, the number of SVGs, CKD, statin usage, EF, AF, and hemoglobin. In this model, statin usage, CHA2DS2-VASc score, time interval after CABG, and the number of SVG were identified as independent predictors of SVG failure (OR: 0.432, 95% CI: 0.248-0.751, p=0.003; OR: 2.203, 95% CI: 1.672-2.902, p<0.001; OR: 1.167, 95% CI: 1.081-1.259, p<0.001; OR: 2.378, 95% CI: 1.745-3.241, p<0.001; respectively). The graphs showing the relationships between the probability of SVG failure and CHA2DS2-VASc score, time interval after CABG, and the number of SVGs were demonstrated in Figure 2. Additionally, the ROC curves were constructed for CHA2DS2-VASc score, time interval after CABG, and the number of SVGs to determine the predictive values for SVG failure in Figure 3. In the ROC analysis, the CHA2DS2-VASc score exhibited an area under the curve (AUC) of 0.796, with a sensitivity of 54.96% and a specificity of 91.55% (Fig. 3). Furthermore, it had a higher AUC value compared to the time interval after CABG and the number of SVGs (AUC: 0.796 vs. AUC: 0.724 vs. AUC: 0.641, respectively), indicating its superior predictive performance. In addition, sensitivity, specificity, positive predictive value, negative predictive value and AUC values of these parameters were demonstrated in Table 4.

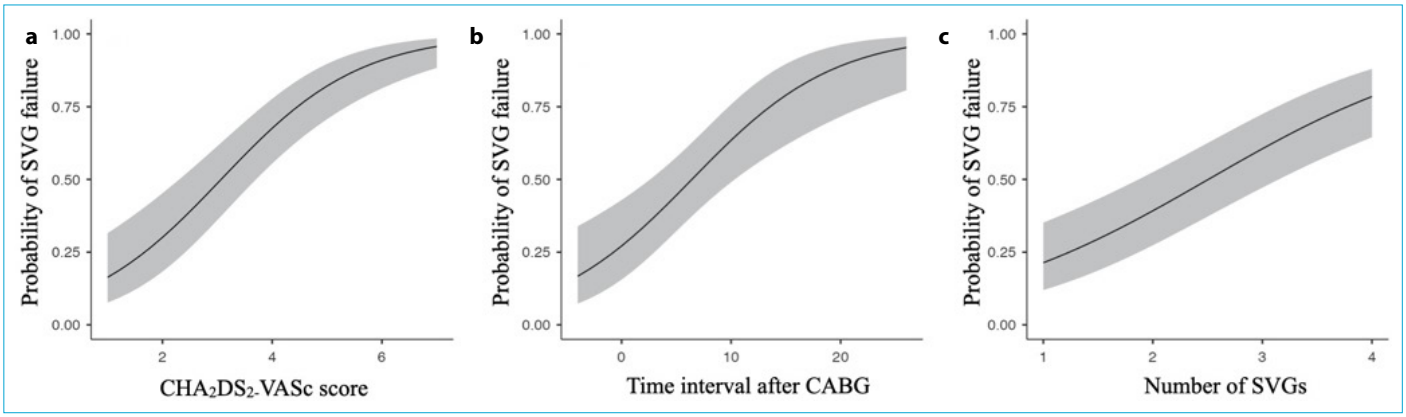

Figure 2. The marginal mean graphs showing the relationship between the probability of SVG failure and CHA2DS2-VASc score **(a)**, time interval after CABG **(b)**, and number of SVG **(c)**.

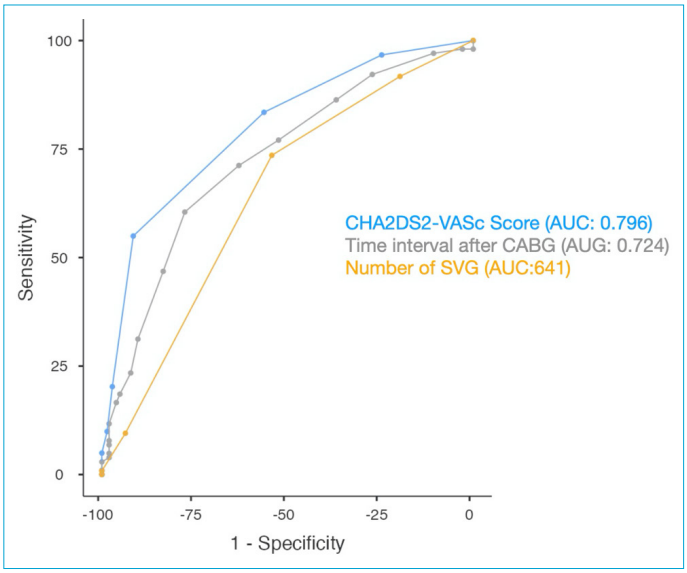

Figure 3. Receiver operating characteristic curves for CHA2DS2-VASc score (blue), time interval after CABG (gray) and number of SVG (yellow) to predict the presence of SVG failure. (AUC, area under the curve; CABG, coronary artery bypass graft; SVG, saphenous vein graft).

Discussion

In this retrospective analysis, we investigated the relationship between the preoperative CHA2DS2-VASc score and the incidence of late SVG failure in patients with NSTEMI who had previously had CABG. According to our research, the CHA2DS2-VASc score was an independent predictor of late SVG failure, as were the number of SVGs, the duration after CABG, and the usage of statins. Interestingly, we found that the CHA2DS2-VASc score had more predictive ability than the other measures evaluated.

SVG failure remains one of the most important problems restricting the advantages of CABG, even if it is still the preferred therapy for left main coronary artery and multivessel disease with an intermediate to high SYNTAX score.[13] However, the use of SVGs in the CABG procedure is still very common. There are three stages of post-CABG graft failure: early (less than one month), intermediate (one month to one year), and late (more than one year). These stages are linked to unfavorable clinical outcomes including mortality, non-fatal myocardial infarction, and the need for recurrent revascularization.[14] Our study did not investigate early graft failure commonly observed at the anastomosis site, which is often associated with technical factors, endothelial damage, and thrombosis, nor did it examine intermediate SVG failure, which is linked to neointimal hyperplasia.[14] On the other hand, atherosclerosis has been blamed in the etiology of late graft failure. Hence, risk factors related to atherosclerosis, such as age, race, gender, hypercholesterolemia, DM, HT, and CKD may contribute to late SVG dysfunction.[14]

Table 4. Assessment of parameters for predicting SVG failure: Sensitivity, specificity, predictive values, and AUC

Parameters	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
CHA2DS2-VASc score	4	54.96	91.55	84.71	70.46	0.796
Time interval after CABG (year)	7	60.49	77.67	72.94	66.39	0.724
Number of SVG	3	73.55	54.23	57.70	70.64	0.641

PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under the curve; CABG: Coronary artery bypass grafting surgery; SVG: Saphenous vein graft.

The CHA2DS2-VASc score is a scoring tool that was first used in clinical practice to assess the risk of stroke or systemic thromboembolism in patients with atrial fibrillation. Previous study has demonstrated that the CHA2DS2-VASc score, which includes conventional atherosclerosis risk factors, can predict atherosclerotic diseases and be associated with their prognosis.[9–11,15] Additionally, Huan et al.[16] showed that in CAD patients, the CHA2DS2-VASc score predicts death. However, there are still few studies showing a relationship between the CHA2DS2-VASc score and late SVG failure, which has been connected to atherosclerosis.[17,18] In the study by Yarlioglues et al.,[18] which was similar to ours, only patients with stable angina were included, and SVG stenosis of 50% or more was defined as SVG failure. In addition, the study by Tasbulak et al.,[17] also similar to ours, included patients with both stable angina pectoris and ACS, whereas our study included only NSTEMI patients. Like other studies, ours clarifies the relationship between the CHA2DS2-VASc score and late SVG failure. Moreover, by encompassing a larger patient cohort compared to existing studies, our investigation broadens the scope of inquiry in this domain.

One of the most important factors predicting SVG failure is the age of the graft.[5,19] As the time interval after CABG increases, SVG failure also increases. Kulik et al.[20] demonstrated that in patients with LDL-C levels <100 mg/dL, the patency rate of SVG was higher in the first year. Additionally, the Post CABG Trial Investigators revealed that a higher dose of lovastatin was associated with less progression of SVG atherosclerosis and a lower incidence of new SVG occlusions.[21] Similarly, we discovered that the number of SVG, statin usage, and the duration following CABG were independent predictors of SVG failure. Furthermore, the CHA2DS2-VASc score in our research had a better predictive value than the period after the SVG count and CABG.

To sum up, the CHA2DS2-VASc score might be a useful instrument for determining the likelihood of late SVG complications. Particularly in patients with high CHA2DS2-VASc scores who are referred for CABG, the consideration of arterial grafts instead of SVGs could be contemplated. However, further research is needed for a better understanding of this relationship and its translation into clinical practice.

Study Limitations

There are some limitations to this study. Firstly, a retrospective design was used in the data collection process; hence there may be potential information gaps that could affect our results. Secondly, our study was conducted at a single center and had a small patient cohort, limiting the generalizability of our findings. Finally, more extensive and thorough research is required to assess the impact of additional possible clinical factors.

Conclusion

The usefulness of this score as a predictor for SVG failure has been highlighted by this study, which showed a link between the CHA2DS2-VASc scoring system and SVG failure in patients following CABG.

Disclosures

Ethics Committee Approval: The Clinical Research Ethics Committee of Kartal Kosuyolu Research and Education Hospital granted approval for this study. (date: 02/07/2024, number: 2024/12/855).

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