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ORIGINAL ARTICLE / ÖZGÜN MAKALE

Prognostic value of CHA_2DS_2-VASc score for the long-term cardiovascular events after coronary artery bypass grafting

Koroner arter baypas greftleme sonrası uzun dönem kardiyovasküler olaylar için CHA_2DS_2-VASc skorunun prognostik değeri

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ABSTRACT

Background: This study aims to investigate the value of the CHA_2DS_2-VASc score in predicting long-term major cardiovascular events following coronary artery bypass grafting.

Methods: Between January 2008 and January 2010, a total of 559 patients (445 males, 114 females; mean age: 62.7±9.1 years; range, 35 to 84 years) who underwent elective coronary artery bypass grafting were retrospectively analyzed. At a mean of 10.7±3.1-year follow-up, major cardiovascular events were considered as the primary endpoint.

Results: The multivariate Cox hazard analysis identified the CHA_2DS_2-VASc score as an independent predictor of major cardiovascular events (hazard ratio: 1.615; 95% confidence interval: 1.038-2.511; p=0.034). The receiver operating characteristic curve analyses revealed that 3.5 was the most optimal cut-off value of the score predicting major cardiovascular events and the patients were divided into two groups accordingly. The Kaplan-Meier analysis demonstrated a significantly higher incidence of major cardiovascular events in proportion to a higher CHA_2DS_2-VASc score (p<0.001).

Conclusion: CHA_2DS_2-VASc score ≥4, which includes many risk factors for cardiovascular events, can be used as an independent predictor of long-term major cardiovascular events after coronary artery bypass grafting.

Keywords: CHA_2DS_2-VASc score, coronary artery bypass grafting, coronary artery disease, major cardiovascular event.

ÖZ

Amaç: Bu çalışmada koroner arter baypas greftleme sonrasında uzun dönem majör kardiyovasküler olayları öngörmede CHA_2DS_2-VASc skorunun değeri araştırıldı.

Çalışma planı: Ocak 2008 - Ocak 2010 tarihleri arasında elektif koroner arter baypas greftleme yapılan toplam 559 hasta (445 erkek, 114 kadın; ort. yaş: 62.7±9.1 yıl; dağılım, 35-84 yıl) retrospektif olarak incelendi. Ortalama 10.7±3.1 yıllık takipte majör kardiyovasküler olaylar primer sonlanım noktası olarak kabul edildi.

Bulgular: Çok değişkenli Cox risk analizi, CHA_2DS_2-VASc skorunun majör kardiyovasküler olayların bağımsız bir öngördürücüsü olduğunu gösterdi (risk oranı: 1.615; %95 güven aralığı: 1.038-2.511; p=0.034). Alıcı işletim karakteristik eğri analizleri majör kardiyovasküler olayları öngören en iyi eşik değerinin 3.5 olduğunu ortaya koydu ve hastalar buna göre iki gruba ayrıldı. Kaplan-Meier analizi, yüksek CHA_2DS_2-VASc skoru ile orantılı anlamlı daha yüksek majör kardiyovasküler olay insidansı gösterdi (p<0.001).

Sonuç: Birçok kardiyovasküler olay risk faktörünü barındıran CHA_2DS_2-VASc skoru ≥4, koroner arter baypas greftleme sonrası uzun dönem majör kardiyovasküler olayların bağımsız bir öngördürücüsü olarak kullanılabilir.

Anahtar sözcükler: CHA_2DS_2-VASc skoru, koroner arter baypas greftleme, koroner arter hastalığı, majör kardiyovasküler olay.

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Coronary artery bypass grafting (CABG) as a cornerstone therapy of multivessel or left main coronary artery disease (CAD) due to its long-lasting survival benefits is the most common open-heart procedure performed worldwide today.[1,2]

As evidenced by guidelines, long-term outcome following CABG is dependent on the prevention of major cardiovascular events (MACEs) which may be reduced by choosing the risky patients and following them closely to apply more aggressive treatment strategies.[3] However, current risk scores of CABG, such as the Society of Thoracic Surgeons (STS) score and European System for Cardiac Operative Risk Evaluation (EuroSCORE), have mainly focused on short-term morbidity and mortality.[4-6] Moreover, Synergy between percutaneous coronary intervention (PCI) with Taxus and Cardiac Surgery (SYNTAX) score was found to be an independent predictor of long-term MACEs following PCI, but not after CABG.[7,8] Thus, the lack of knowledge about which patients should be closely monitored for MACEs following CABG needs to be overcome.

The CHA_2DS_2-VASc score was developed to evaluate the risk for long-term ischemic stroke in patients with atrial fibrillation (A-fib),[9] using risk factors of ischemic stroke in patients with CAD, based on large cohort studies.[10,11] Moreover, the difference of the CHA_2DS_2-VASc (congestive heart failure [HF], hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65-74, and sex category [female]) over the older CHADS2 (cardiac failure, hypertension, age, diabetes mellitus [DM], stroke [doubled]) score is additional CAD risk factors like female sex and vascular disease. Not surprisingly, as its all components are traditional risk factors of atherosclerosis, the predictive value of this score has been recently shown on mid-term myocardial infarction (MI) following PCI and on short-term ischemic stroke after PCI and CABG, even in non-A-Fib population.[12] However, it is not clear that these findings are also true for long-term MACEs in CABG patients. The usefulness of the CHADS2 score for predicting long-term cardiovascular mortality in CABG patients has been reported; however, the literature is lacking in the predictive value of the newer CHA_2DS_2-VASc score.[13] The meta-analysis of Zhu et al.[14] showed the better discriminative capacity of the CHA_2DS_2-VASc *vs*. CHADS2 score. In the present study, we aimed to investigate the value of the CHA_2DS_2-VASc score in predicting long-term MACEs following CABG.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Istinye University and Bursa VM Medical Park Hospital, Department of Cardiovascular Surgery between January 2008 and January 2010. Patients who underwent elective isolated on-pump CABG were enrolled according to the inclusion and exclusion criteria. The inclusion criteria were as follows: triple-vessel disease, severe left main stem artery stenosis or left main equivalent disease, and two-vessel disease with proximal left anterior descending artery (LAD) stenosis. Exclusion criteria were as follows: critical preoperative state (need for inotropic drug support or intra-aortic balloon pumping [IABP], acute renal failure, need for respiratory support, history of preoperative cardiopulmonary resuscitation), previous heart surgery, MI within three weeks (cTnI>0.01 ng/mL) and missing data (n=51). Finally, 559 patients (445 males, 114 females; mean age: 62.7±9.1 years; range, 35 to 84 years) were included.

Patients characteristics

Preoperative characteristics of the patients included age, sex, smoking status, hypertension, hyperlipidemia, DM, family history of CAD, obesity (body mass index >30 kg/m^2), chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), asymptomatic carotid stenosis, history of cerebrovascular accident (CVA), history of MI, unstable angina pectoris (USAP), history of PCI, left ventricular (LV) dysfunction, mild mitral insufficiency, the number of vessel disease, and presence of left main coronary artery (LMCA) stenosis, EuroSCORE, and CHA_2D_2-VASc score.

The CHA_2DS_2-VASc score was calculated by assigning 1 point each for congestive HF, hypertension, age 65 to 74 years, DM, vascular disease (history of MI or PCI, peripheral or CAD), and female sex and 2 points each for previous CVA, or age ≥75 years.[9]

The diagnosis of DM was based on the previous history of diabetes or fasting plasma glucose ≥126 mg/dL or hemoglobin A1c ≥6.5%. The diagnosis of dyslipidemia was based on the previous history of total cholesterol ≥200 mg/dL or low-density lipoprotein (LDL) ≥130 mg/dL. Vessel disease was defined as stenosis of >50% of major epicardial coronary arteries. Estimated creatinine clearance (CrCl) was calculated using the Cockcroft-Gault formula: CrCl (mL/min) = ([140-age] × weight [kg])/(serum creatinine [mg/dL] × 72) (× 0.85 for women) from baseline blood samples. The diagnosis

Table 1. Cox Regression Analysis for Independent Predictors of Long-Term MACEs

	Univariate analysis			Multivariate analysis		
Characteristics	HR	95% CI	*p*	HR	95% CI	*p*
Age (year)	1.037	1.023-1.052	<0.001*	1.006	0.983-1.031	0.59
Sex						
Female	1.581	1.201-2.082	0.001*	1.067	0.704-1.616	0.76
Active smoker	0.817	0.637-1.048	0.11			
Hypertension	1.450	1.135-1.853	0.003*	1.185	0.852-1.647	0.31
Hyperlipidemia	0.820	0.619-1.086	0.16			
Diabetes mellitus	1.253	0.975-1.609	0.07			
IDDM	1.577	1.066-2.335	0.023*	1.057	0.634-1.761	0.83
Family history of CAD	0.770	0.583-1.017	0.06			
Obesity	1.036	0.789-1.361	0.79			
COPD	1.269	0.804-2.002	0.3			
PVD	1.690	1.096-2.607	0.018*	1.284	0.746-2.210	0.36
Carotid stenosis	1.779	1.329-2.383	<0.001*	1.253	0.822-1.910	0.29
History of CVA	1.563	1.134-2.154	0.006*	1.382	0.751-2.543	0.29
Previous A-fib	1.517	0.567-4.057	0.40			
Previous MI	1.520	1.177-1.964	0.001*	1.419	1.007-2.000	0.045*
USAP	0.972	0.747-1.263	0.83			
History of PCI	1.068	0.707-1.612	0.75			
CrCL	0.992	0.988-0.996	0.001*	0.997	0.992-1.002	0.24
Hb level	0.892	0.841-0.945	0.001*	0.917	0.857-0.981	0.012*
LV dysfunction	1.288	1.003-1.653	0.048*	1.011	0.646-1.581	0.96
Mild mitral failure	1.124	0.776-1.626	0.53			
LMCA stenosis	1.13	0.854-1.529	0.36			
Number of vascular disease	1.213	0.863-1.705	0.26			
EuroSCORE II	1.093	1.064-1.122	<0.001*	1.037	0.978-1.099	0.22
CHA_2DS_2-VASc	2.196	1.719-2.805	<0.001*	1.615	1.038-2.512	0.034*
CPB time	1.010	0.995-1.026	0.2			
Number of distal anastomosis	0.995	0.857-1.154	0.94			
Incomplete revascularization	0.795	0.622-1.439	0.79			
Endarterectomy	1.064	0.727-1.556	0.75			
Low cardiac output	2.837	0.397-20.267	0.29			
Prolonged respiratory support	1.469	0.547-3.947	0.44			
Postoperative A-fib	1.075	0.746-1.549	0.69			
Number of blood unit	1.153	1.065-1.248	0.001*	1.025	0.919-1.144	0.65
Postoperative renal failure	1.486	1.070-2.063	0.018*	1.151	0.777-1.705	0.48
Pulmonary complication	1.045	0.712-1.532	0.82			
Chest tube drainage	1.000	1.000-1.001	0.74			
Hospital stay	1.052	0.996-1.112	0.06			

HR: Hazard ratio; CI: Confidence interval; IDDM: Insulin-dependent diabetes mellitus; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; PVD: Peripheral vascular disease; CVA: Cerebrovascular accident; A-fib: Atrial fibrillation; MI: Myocardial infarction; USAP: Unstable angina pectoris; PCI: Percutaneous coronary intervention; CrCL: Creatinine clearance; Hb: Hemoglobin; LV: Left ventricle; LMCA: Left main coronary artery; EuroSCORE II: European System for Cardiac Operative Risk Evaluation; CPB: Cardiopulmonary bypass; * Statistically significant difference.

of COPD was based on the previous history of bronchodilator treatment or the forced expiratory volume in 1 sec (FEV1)/forced vital capacity (FVC) ratio <0.70. Carotid stenosis was defined as a ≥50% narrowing of the internal carotid artery. Peripheral vascular disease was defined as an arterial disease affecting the vasculature of extremities with a ≥50% diameter narrowing or history of intervention. A LV dysfunction was defined as an ejection fraction of <0.50).

Pre- and postoperative data were retrospectively collected from hospital records. Incomplete revascularization was defined as untreated diameter stenosis of more than 50% in a major epicardial coronary artery. Drainage was defined as the amount of drainage collected in the first 24 h. Blood transfusion was defined as the sum of the blood units used during the hospital stay. Perioperative MI was defined as cardiac troponin I (cTnI) >5 µg/L during hospitalization. Renal complication was defined as an increase of at least ≥100% in basal serum creatinine. A pulmonary complication was defined for pleural effusion, atelectasis, phrenic nerve palsy, diaphragmatic dysfunction, pneumonia, acute respiratory distress syndrome, pneumothorax, or chylothorax. Prolonged mechanical ventilation time was defined as total intubation time greater than 10 h. A neurological complication included new transient ischemic attack, stroke or encephalopathy occurring in the perioperative period. Early reoperation was defined as any hospitalization due to CABG-related complications (such as sternal dehiscence, mediastinitis) or cardiovascular problems (such as MI, congestive HF, rhythm disturbance, neurological complications, pulmonary embolism).

Surgical procedure

Following median sternotomy, the left internal thoracic artery and other conduits were prepared simultaneously. Heparin was administered to keep the activated clotting time (ACT) greater than 450 sec. All procedures were performed without using an aortic cross-clamping and cardioplegia. Cardiopulmonary bypass (CPB) was established with an ascending aortic arterial cannula and a right atrial two-stage venous cannula, using a membrane oxygenator and a roller pump. All patients were cooled to 34°C. The mean arterial blood pressure was maintained in the range of 60 to 90 mmHg. Distal anastomoses were performed by end-to-side or side-to-side techniques with a running 7/0 Prolene® suture, using a myocardial stabilizer device (Octopus IV, Medtronic Inc., Minneapolis, MN, US). Proximal anastomoses were performed using a 6/0 Prolene® suture during the heating period using an aortic side-clamp. After completion of CPB and cannula removal, heparin was neutralized with protamine providing an ACT of fewer than 160 sec. Acetylsalicylic acid at a dose of 100 mg and subcutaneous enoxaparin were initiated on the postoperative 24 h.

Follow-up

Long-term follow-up was obtained through outpatient clinic visits, hospitals records and phone calls. All-cause mortality (patient death reported by relatives or hospital records) and MACE (MI, repeated CABG or PCI, need for dual-chamber pacemaker or rehospitalization due to decompensated HF, stroke, cardiac-related or sudden death) were evaluated.

The primary endpoint of this study is to identify the predictive value of the CHA_2DS_2-VASc score on long-term MACE following CABG.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in

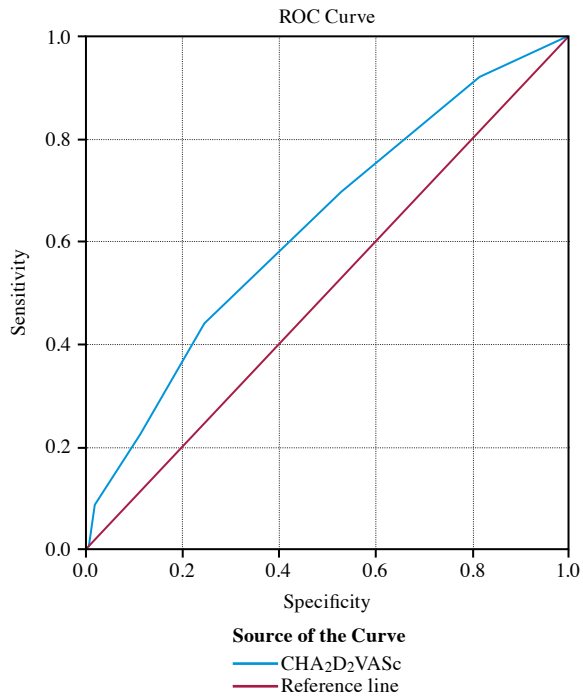

Figure 1. ROC curve analysis.

The diagonal represents the no-effect line (AUC=0.50), with curves above this line representing increasing diagnostic accuracy. CHA_2DS_2-VASc score accurately predicted MACE (AUC, 0.63; 95% CI: 0.583-0.675; p<0.001). The optimal cut-off to predict MACE is 3.5 with a sensitivity of 44.6% and specificity of 75.3%. AUC: Area under the curve.

Table 2. Baseline characteristics according to CHA_2DS_2-VASc groups

	Overall (n=559)			CHA_2D_2-VASc <4 (n=369)			CHA_2D_2-VASc ≥4 (n=190)			
Characteristics	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
CHA_2DS_2-VASc			3±1.36			2.20±0.75			4.56±0.83	<0.001*
EuroSCORE II			3.45±3.25			2.46±2.01			5.46±4.22	<0.001*
Age (year)			62.7±9.1			59.7±8.4			68.4±7.7	<0.001*
Sex										
Female	114	20.4		31	8.4		83	43.7		<0.001*
Active smoker	221	39.5		180	48.8		41	21.6		<0.001*
Diabetes mellitus	196	35.1		75	20.3		121	63.7		<0.001*
IDDM	48	8.6		16	4.3		32	16.8		<0.001*
Hypertension	287	51.3		137	37.1		150	78.9		<0.001*
Hyperlipidemia	151	27		91	24.7		60	31.6		<0.001*
Family history of CAD	155	27.7		110	29.8		45	23.7		0.12
Obesity (BMI ≥30)	157	28.4		87	23.6		70	36.8		0.001*
CrCL			100.75±34.66			105.41±32.55			91.71±36.89	<0.001*
Hb level			11.03±2.32			11.2±2.41			10.68±2.07	0.035*
COPD	37	6.6		22	6		15	7.9		0.38
PVD	27	4.8		16	4.4		11	5.8		0.45
Carotid stenosis	94	16.8		47	12.7		47	24.7		<0.001*
History of CVA	21	3.8		1	0.3		20	10.5		<0.001*
Previous A-fib	9	1.6		4	1.1		5	2.6		0.16
History of MI	159	28.4		101	27.4		58	30.5		0.43
USAP	177	31.7		107	29		70	36.8		0.06
Previous PCI	49	8.8		37	10		12	6.3		0.14
LV dysfunction	185	33.1		92	24.9		93	48.9		<0.001*
Mild mitral insufficiency	65	11.6		33	8.9		32	16.8		0.006*
LMCA stenosis	120	21.5		79	21.4		41	21.6		0.96
Three vessel disease	500	89.4		318	86.2		182	95.8		0.001*
Number of Vd			2.87±0.38			2.84±0.4			2.94±0.26	0.001*

SD: Standard deviation; EuroSCORE II: European System for Cardiac Operative Risk Evaluation; IDDM: Insulin-dependent diabetes mellitus; CAD: Coronary artery disease; BMI: Body mass index; CrCL: Creatinine clearance; Hb: Hemoglobin; COPD: Chronic obstructive pulmonary disease; PVD: Peripheral vascular disease; CVA: Cerebrovascular accident; A-fib: Atrial fibrillation; MI: Myocardial infarction; USAP: Unstable angina pectoris; PCI: Percutaneous coronary intervention; LV: Left ventricle; LMCA: Left main coronary artery; Vd: Vascular disease; * Statistically significant difference.

mean ± standard deviation (SD), while categorical variables were expressed in number and frequency. The Mann-Whitney U test was used to compare nonparametric continuous variables, the Student t-test was used to compare parametric continuous variables, and the chi-square test was used to compare categorical variables. The cumulative survival curves for long-term MACEs were constructed with the use of the Kaplan-Meier method, while differences between the CHA_2DS_2-VASc groups were evaluated with log-rank tests. The receiver operating characteristics (ROC) curve was used to detect the optimal cut-off value for predicting MACEs. Cox regression analysis was performed to determine independent predictors of MACE, with those variables with a p value of <0.05 in the univariate analysis included in the stepwise multivariate model. The hazard ratio (HR) and 95% confidence intervals (CIs) were calculated.

The association between variables was tested using Spearman or Pearson correlation coefficient. A two-tailed *p* value of <0.05 was considered statistically significant.

RESULTS

In the univariate analyses, age, female sex, hypertension, insulin-dependent diabetes mellitus (IDDM), PVD, asymptomatic carotid artery stenosis, history of CVA, previous MI, CrCL, hemoglobin (Hb) level, LV dysfunction, EuroSCORE II, CHA_2D_2-VASc, the mean number of red blood cell transfusion units, renal complications were associated with an increased incidence of MACEs. While assessing the independent effect of all potential risk factors on MACE occurrence in multivariate analysis, CHA_2DS_2-VASc (HR: 1.615, <95% CI: 1.038-2.512; p=0.034), Hb level (HR: 0.917, <95% CI: 0.857-0.981; p=0.012) and previous MI (HR: 1.419, <95% CI: 1.007-2.000; p=0.045) were identified as independent predictors of MACEs (Table 1).

The ROC curve of CHA_2DS_2-VASc revealed an area under the curve (AUC) value of 0.63 (95% CI:

Table 3. Peri- and postoperative characteristics of the patients stratified by CHA_2DS_2-VASc groups

	Overall (n=559)			CHA_2DS_2-VASc <4 (n=369)			CHA_2DS_2-VASc ≥4 (n=190)			
Characteristics	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
CPB time (min)			94.72±23.42			93.41±23.54			97.04±23.55	0.49
Number of distal anastomoses			3.64±0.79			3.66±0.79			3.6±0.8	0.22
Incomplete revascularization	9	8.8		29	7.9		20	10.5		0.29
Endarterectomy	63	11.3		42	11.4		21	1.1		0.9
ICU stay (h)			23.26±52.19			20.34±15.94			28.93±86.6	<0.001*
Drainage (mL/24 h)			533.09±312.5			531.33±310.45			536.55±319	0.78
Blood transfusion (unit)			1.43±1.62			1.11±1.52			2.03±1.65	<0.001*
Inotropic support	32	5.7		15	4.1		17	8.9		0.018*
LCO	5	0.9		3	0.8		2	1.1		0.77
Peroperative MI	56	10		35	9.5		21	11.1		0.56
Renal complication	84	15		36	9.8		48	25.3		<0.001*
Prolonged respiratory support	13	2.3		6	1.6		7	3.7		0.12
Pulmonary complication	13	2.3		6	1.6		7	3.7		0.12
Mediastinitis	5	0.9		1	0.3		4	2.1		0.029*
Neurological complication	41	7.3		15	4.1		26	13.7		<0.001
Delirium	19	3.4		8	2.2		11	5.8		0.025*
TIA	22	3.9		7	1.9		15	7.9		0.001*
Stroke	3	0.5		0	0		3	1.6		0.016*
A-Fib	76	13.6		36	9.8		40	21.1		<0.001*
Prolonged A-Fib duration	12	2.1		5	1.4		7	3.7		0.07
Early re-operation	14	2.5		6	1.6		8	4.2		0.06
Hospital stay (days)			5.91±2.84			5.53±1.39			6.65±4.38	<0.001*
Early rehospitalization	34	6.1		12	3.3		22	11.6		<0.001*
In hospital mortality	7	1.3		1	0.3		6	3.2		0.004*

SD: Standard deviation; CPB: Cardiopulmonary bypass; ICU: Intensive care unit; LCO: Low cardiac output; MI: Myocardial infarction; TIA: Transient ischemic attack; A-fib: Atrial fibrillation; * Statistically significant difference.

0.583-0.675, p<0.001) and the most optimal cut-off value to predict the MACE was ≥3.5 with 44.6% sensitivity and 75.3% specificity (Figure 1). The patients were divided into two groups according to this cut-off value. Group 1 consisted of 369 patients with CHA_2DS_2-VASc score <4, while Group 2 consisted of 190 patients with CHA_2DS_2-VASc score ≥4.

Baseline characteristics are shown in Table 2. According to the components of the CHA_2DS_2-VASc score, Group 2 patients were significantly older (p<0.001), more diabetic (p<0.001), predominantly female (p<0.001) and more hypertensive (p<0.001) or had more LV dysfunction (p<0.001), asymptomatic carotid stenosis (p<0.001), and history of CVA (p<0.001). Moreover, Group 2 consisted of significantly more patients with IDDM (p<0.001), obesity (p<0.001), and hyperlipidemia (p<0.001). Furthermore, Group 2 patients had a significantly lower CrCL (p<0.001) and lower Hb level (p=0.035). Additionally, Group 2 had significantly more mild mitral insufficiency (p=0.006) and three-vessel disease (p<0.001) or higher mean number of vessel disease (p<0.001). Contrarily, the lower CHA_2D_2-VASc group included significantly more active smokers (p<0.001).

Peri- and early postoperative characteristics of the patients are shown in Table 3. The operative characteristics of the two groups were similar regarding CPB time, incomplete revascularization, mean number of distal anastomosis and endarterectomy. Moreover, no significant difference was found between groups in term of amount of drainage, low cardiac output (LCO), perioperative MI, prolonged respiratory support, pulmonary complications, A-fib duration, and early reoperation. However, patients with higher CHA_2DS_2-VASc score required more blood transfusion (p<0.001) or inotropic support (p=0.018) and showed significantly more renal complication (p<0.001), neurological complication (p<0.001), perioperative A-fib (p<0.001), and mediastinitis (p=0.029). Furthermore, higher CHA_2DS_2-VASc score were associated with prolonged intensive care unit (ICU) stay (p<0.001), and hospital stay (p<0.001), or increased incidence of early rehospitalization (p<0.001) and in-hospital mortality (p=0.004).

Long-term follow-up characteristics are shown in Table 4. Patients in Group 2 showed a significantly lower MACE-free survival (Group 1, 126.45±37.08 months; Group 2, 98.63±48.29 months; p<0.001). Accordingly, the higher CHA_2D_2-VASc score was related to significantly more cumulative MACE at one year (p<0.001), at five years (p<0.001), at 10 years (p<0.001). Moreover, patients with higher CHA_2DS_2-VASc score showed higher all-cause mortality (p<0.001), cardiovascular mortality (p<0.001), MI (p<0.001), late reintervention (p=0.003), and stroke

Table 4. Long-term outcomes according to CHA_2DS_2-VASc groups

	Overall (n=559)			CHA_2DS_2-VASc <4 (n=369)			CHA_2DS_2-VASc ≥4 (n=190)			
Characteristics	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Mean follow-up (month)			128.85±38.22			137.88±29.28			111.32±46.65	<0.001*
MACE free survival			116.99±43.25			126.45±37.08			98.63±48.29	<0.001*
MACE 1 year	18	3.2		4	1.1		14	7.4		<0.001*
MACE 5 years	59	10.6		23	6.2		36	18.9		<0.001*
MACE 10 years	198	35.4		96	26		102	53.7		<0.001*
MACE >10 years	263	47		147	39.8		116	61.1		<0.001*
Myocardial infarction	189	33.8		104	28.2		85	44.7		<0.001*
Stroke	58	10.4		28	7.6		30	15.8		0.003*
Late reintervention	110	19.7		60	16.3		50	26.3		0.003*
All-cause mortality	223	39.9		112	30.4		111	58.4		<0.001*
Cardiovascular mortality	170	30.4		78	21.1		92	48.4		<0.001*
Cardiac mortality	133	23.8		59	16		74	38.9		<0.001*
Non-cardiovascular mortality	53	9.5		34	9.2		19	10		0.68

SD: Standard deviation; CPB: Cardiopulmonary bypass; ICU: Intensive care unit; LCO: Low cardiac output; TIA: Transient ischemic attack; A-fib: Atrial fibrillation; * Statistically significant difference.

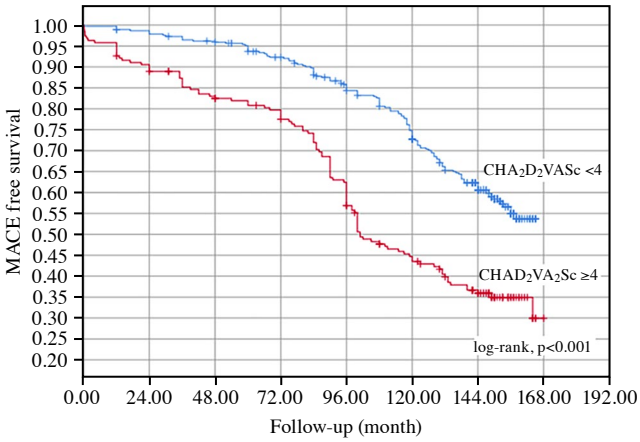

Figure 2. Kaplan-Meier estimates of MACE-free survival (p<0.001 by the log-rank test).

MACE: Major cardiovascular event.

(p=0.003). However, non-cardiovascular mortality did not differ between the groups (p=0.68). Kaplan-Meier analysis of freedom from MACE revealed significantly lower MACE free survival in Group 2 (Group 1, 60.2%; Group 2, 38.9%; p<0.001 by the log-rank test) (Figure 2).

DISCUSSION

In the present study, we investigated the value of the CHA_2DS_2-VASc score in predicting long-term MACEs following CABG. First and foremost, long-term MACE after CABG was significantly predicted by a high CHA_2DS_2-VASc score. Second, long-term cardiovascular mortality following CABG was correlated with a high CHA_2DS_2-VASc score, whereas non-cardiovascular mortality was not.

Care after coronary revascularization is primarily focused on preventing recurrent MACE with an incidence as high as 51% at 10 years.[4,15] However, a standard evaluation tool for predicting the long-term MACE for this population is lacking. Thus, a practical tool is needed that effectively stratifies the risk of long-term cardiovascular events after CABG, to personalize treatment strategies.

The CHA_2DS_2-VASc score, CHADS2 score and CHA_2DS_2-VASc-HS score comprise clusters of common cardiovascular risk factors associated with thromboembolism. Unsurprisingly, strong correlations are reported among CHA_2DS_2-VASc-HS score, which incorporated hyperlipidemia and smoking, and severity of CAD,[16] CHADS2 scores and long-term all-cause mortality following CABG,[13] CHA_2DS_2-VASc score and post-procedural ischemic stroke after PCI and CABG,[12] CHADS2 score and long-term mortality after acute coronary syndrome,[17] CHA_2DS_2-VASc score and in-hospital MACE.[18] However, evidence regarding usage of CHA_2DS_2-VASc score for risk stratification after CABG in the long-term is lacking.

In the current study, the CHA_2D_2-VASc score was an independent predictor of long-term MACE, unlike EuroSCORE II. This finding can be explained by our study protocol which exclude half of the EuroSCORE II parameters which focused on in-hospital follow-up such as urgency, recent MI, critical preoperative stat, redo or combined surgery. Accordingly, Barili et al.[19] reported that EuroSCORE II performance fades for mortality at follow-up longer than 30 days. On the contrary, the CHA_2D_2-VASc score was created and approved for long-term stroke risk prediction and all of its components like HF, age, diabetes, history of stroke, vascular disease, and female sex were mainly predictors of CAD severity and course of MACE.[9]

Besides its components, we revealed that the high CHA_2DS_2-VASc score was related to factors pointing to severity and complexity of atherosclerosis, such as dyslipidemia, decreased CrCl levels, similar to the previous CHAD2 score studies.[13,20] As the SHINANO registry revealed CHA_2DS_2-VASc score ≥3 was associated with the increased Syntax score, we also found that mean vascular disease was greater in CHA_2DS_2-VASc score ≥4.[21] Moreover, we revealed that a high CHA_2DS_2-VASc score was associated with higher body mass index (BMI). According to the SHINANO registry, our study showed Hb level and CHA_2D_2-VASc score were inversely related, which has been recently shown as an independent predictor of MACE.[22] In the light of all these facts, it can be speculated that the CHA_2DS_2-VASc score is strongly correlated with the severity of CAD which increases the vulnerability to MACE.

Despite similar operative data such as CPB time, the number of distal anastomoses, endarterectomy or incomplete revascularization rate, patient with high CHA_2D_2-VASc score needed more perioperative inotropic support which might be related to the HF component of the score. Unsurprisingly, by its primary purpose and previous studies, high CHA_2DS_2-VASc score was found to be correlated with increased postoperative neurological complication and A-fib rate.[9,14] Moreover, the higher CHA_2DS_2-VASc score group showed more postoperative renal complication according to the lower preoperative CrCL level, consistent with the literature.[18] Although no significant difference was found in terms of postoperative drainage, a higher

CHA_2DS_2-VASc score was related to significantly more blood transfusion. Even if this finding may also be affected by decreased basic Hb levels in the same group of patients, the association of blood transfusion with mortality has been clearly proven.[23] Our study revealed that patients with higher CHA_2DS_2-VASc score were more likely to have mediastinitis. Although it is considered that this finding may be affected by basic BMI, recent literature showed the same tendency independent from BMI.[18] As a sum of all these morbidities, unsurprisingly, a high CHA_2DS_2-VASc score was found to be associated with a prolonged hospital stay, ICU stay, and increased rehospitalization. Furthermore, similar to the recent studies, we also revealed the relationship between increased in-hospital mortality and high CHA_2DS_2-VASc score.[18]

As shown in previous publications with PCI, patients with high CHA_2DS_2-VASc scores showed significantly lower MACE-free survival, and also higher MACE at one year, at five years, and 10 years following CABG.[20,21,24] Myocardial infarction, stroke and reintervention were detected significantly more in patients with high CHA_2DS_2-VASc scores. Correlated to the report of Lu et al.[13] evaluating CHADS2 score, our study showed a similar correlation between cardiovascular mortality and high CHA_2DS_2-VASc score. In addition, as the non-cardiovascular mortality was not found to be correlated with the score, the relation between all-cause mortality and CHA_2DS_2-VASc score seems to be mainly affected by cardiovascular mortality.

The SHINANO registry, as a multi-center, prospective study, revealed a CHA_2DS_2-VASc score ≥5 was predictive for long-term MACEs after PCI.[21] Moreover, the CHA_2DS_2-VASc score ≥4 in patients with HF without AF was found to be an absolute risk for thromboembolic complications compared to patients with AF.[25] In this study, we identified, for the first time, that a CHA_2DS_2-VASc score ≥4 was the optimal value to predict long-term MACEs following elective isolated CABG.

The limitations to this study are the reflection of a single-center experience and retrospective design. However, our population consisted of homogeneous, consecutive unselected CABG patients, relevant to most patients undergoing CABG in the general population. Moreover, all patients were submitted to the same technique, under the same experienced surgeon supervision; therefore, the technical differences which may interact with the incidence of MACE were excluded.

In conclusion, a CHA_2DS_2-VASc score ≥4 is independently associated with the risk of major cardiovascular events following coronary artery bypass grafting in the long term. This practical predictor may help to identify individuals at high risk for adverse outcomes and candidates who may require more aggressive management strategies in daily practice. Further multi-center, large-scale, prospective, randomized-controlled trials are needed to confirm these results.

Ethics Committee Approval: The study protocol was approved by the Istinye University Human Research Ethics Committee (date: 22.12.2021, no: 21-113). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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