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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Predictive value of newly defined CHA_2DS_2-VASc-HSF score for severity of coronary artery disease in ST segment elevation myocardial infarction

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Abstract

Background: $CHADS_2$ and CHA_2DS_2-VASc scores are widely used in clinical practice and include similar risk factors for the development of coronary artery disease (CAD). It is known that the factors comprising the newly defined CHA_2DS_2-VASc-HSF score promote atherosclerosis and are associated with severity of CAD.

Aim: To investigate the association of the CHA_2DS_2-VASc-HSF score with the severity of CAD as assessed by SYNTAX score (SxS) in patients with ST segment elevation myocardial infarction (STEMI).

Methods: A total of 454 consecutive patients with STEMI (males 79%, mean age 57.3 ± 12.9 years), who underwent primary percutaneous coronary intervention were included in our study. The patients were divided into three groups according to the SxS tertiles: low SxS group (SxS < 14; 151 patients), intermediate SxS group (SxS 14–20; 152 patients), and high SxS group (SxS ≥ 21; 151 patients).

Results: The $CHADS_2$, CHA_2DS_2-VASc, and CHA_2DS_2VASc-HSF scores were found to be significantly different among the SxS groups ($p < 0.001$, $p < 0.001$, and $p < 0.001$). After multivariate analysis, the CHA_2DS_2-VASc-HSF score was associated with high SxS (odds ratio [OR] 1.258, 95% confidence interval [CI] 1.026–1.544; $p = 0.028$) together with age (OR 1.032, 95% CI 1.013–1.050; $p = 0.001$) and ejection fraction (OR 0.927, 95% CI 0.901–0.955; $p < 0.001$).

Conclusions: A newly diagnosed CHA_2DS_2-VASc-HSF score predicts the severity of atherosclerosis in patients with STEMI.

Key words: $CHADS_2$-VASc-HSF score, severity, coronary artery disease, STEMI

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INTRODUCTION

The $CHADS_2$ and CHA_2DS_2-VASc scores are clinical predictors used to evaluate the risk of cardiac thromboembolism and to guide antithrombotic therapy [1, 2]. $CHADS_2$ and CHA_2DS_2-VASc scores are widely used in clinical practice and include similar risk factors for the development of coronary artery disease (CAD). These scores have been demonstrated to have predictive value in terms of the risk of death after stroke [3], the risk of stroke or death after coronary artery bypass grafting (CABG) [4], and the risk of stroke and death in patients with stable CAD [5] and acute coronary syndrome [6].

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Table 1. CHADS2-VASc-HSF score

C	Congestive heart failure	1 point
H	Hypertension	1 point
A2	Age > 75 years	2 point
D	Diabetes mellitus	1 point
S2	Previous stroke or TIA	2 point
V	Vascular disease	1 point
A	Age 65–74 years	1 point
Sc	Sex category (male gender)	1 point
H	Hyperlipidaemia	1 point
S	Smoking	1 point
F	Family history of CAD	1 point

Maximum score = 12 points; CAD — coronary artery disease; TIA — transient ischaemic attack

Recently, Cetin et al. [7] reported that the $CHADS_2$, CHA_2DS_2-VASc, and newly defined CHA_2DS_2-VASc-HS scores could predict CAD severity using the Gensini score in patients who underwent diagnostic coronary angiography [7]. The CHA_2DS_2-VASc-HSF score was formulated [heart failure (signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction), hypertension (HT) (defined as measurements of systolic and diastolic blood pressure ≥ 140/90 mm Hg or taking antihypertensive medications), age, diabetes mellitus (DM) (defined as a fasting blood glucose level > 126 mg/dL or blood glucose ≥ 200 mg/dL or using antidiabetic drugs), previous ischaemic stroke or transient ischaemic attack (TIA), vascular disease (defined as myocardial infarction [MI] and peripheral artery disease including prior revascularisation, amputation or angiographic evidence or aortic plaque), male sex, hyperlipidaemia (defined as increased level of low density lipoprotein cholesterol (LDL-C) according to the National Cholesterol Education Program-3 recommendations and history of using lipid lowering medications), smoking status (defined as smoking > 10 cigarettes a day for at least one year without a quit attempt), and family history of CAD (defined as MI before 55 years of age for men or 65 years of age for women in first-degree relatives)] (Table 1). Compared to the CHA_2DS_2-VASc score, male gender instead of female as sex category, hyperlipidaemia, smoking, and family history of CAD was added in this score.

Our aim was to investigate the association of the CHA_2DS_2-VASc-HSF score with the severity of CAD as assessed by SYNTAX score (SxS) in patients with ST segment elevation MI (STEMI).

METHODS

A total of 454 consecutive patients with STEMI (males 79%, mean age 57.3 ± 12.9 years), who underwent primary percutaneous coronary intervention (PCI) were included in our study. STEMI was defined by the criteria formulated by the European Society of Cardiology: new ST elevation at the J point in leads V2–V3 ≥ 0.2 mV in men ≥ 40 years, ≥ 0.25 mV in men < 40 years, ≥ 0.15 mV in women, ≥ 0.1 mV in the other contiguous leads and also new left bundle branch block with an increase of cardiac biomarker values [8]. Patients with a history of CABG surgery, infectious or inflammatory disease, severe liver or renal disease, neoplasm, or haematological disorders were excluded.

Detailed medical history and physical, electrocardiographic, and echocardiographic examinations were performed, and the following components of the scores were obtained for each patient: chronic heart failure (CHF) (defined signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction), HT (defined as measurements of systolic and diastolic blood pressure ≥ 140/90 mm Hg or taking antihypertensive medications), age, DM (defined as a fasting blood glucose level >126 mg/dL or blood glucose ≥ 200 mg/dL or using antidiabetic drugs), previous ischaemic stroke or TIA, vascular disease (defined as MI and peripheral artery disease including prior revascularisation, amputation or angiographic evidence or aortic plaque), gender, hyperlipidaemia (defined as increased level of LDL-C according to the National Cholesterol Education Program-3 recommendations and history of using lipid lowering medications), smoking status (defined as smoking > 10 cigarettes a day for at least one year without a quit attempt), and family history of CAD (defined as MI before 55 years of age for men or 65 years of age for women in first-degree relatives).

Coronary angiography was performed using the Judkins technique (Siemens Axiom Artis zee 2011; Siemens Healthcare, Erlangen, Germany). Coronary angiograms and also SxS were examined pre-primary PCI by two experienced interventional cardiologists who were blinded to the clinical characteristics and laboratory results of the patients. From the baseline diagnostic angiogram, each coronary lesion producing at least 50% diameter stenosis in vessels of at least 1.5 mm was evaluated separately and added together to provide the total SxS; this is available on the SxS website (http://www.syntaxscore.com) [9]. In case of disagreement, the opinion of a third cardiologist was sought and the final decision was made by consensus. The patients were divided into three groups according to the SxS tertiles: low SxS group (SxS < 14; 151 patients), intermediate SxS group (SxS 14–20; 152 patients), and high SxS group (SxS ≥ 21; 151 patients).

Transthoracic echocardiography was performed for each patient before hospital discharge (Vivid 7 GE Medical System; GE Healthcare, Horten, Norway). Left ventricular ejection fraction (LVEF) was measured using Simpson's method.

Fasting venous blood samples on follow-up were obtained from all patients to evaluate their plasma levels of fasting blood glucose, total cholesterol, high-density lipoprotein cholesterol, LDL-C, triglyceride, uric acid, creatinine, and blood count.

Measurements of haematological parameters were performed by an automatic blood counter (A Sysmex XE-2100, Symex, Kobe, Japan). The other laboratory parameters were measured using an autoanalyser (Roche Diagnostic Modular Systems, Tokyo, Japan).

The $CHADS_2$ score was the sum of 1 point each for CHF, HT, age ≥ 75 years, and DM and 2 points for prior stroke or TIA. The CHA_2DS_2-VASc score was the sum of 1 point each for CHF, HT, age 65–74 years, DM, vascular disease, and female gender and 2 points each for prior stroke or TIA and age ≥ 75 years. The newly formulated CHA_2DS_2-VASc-HSF score consists of CHF, HT, age ≥ 75 years (double score), DM, previous stroke/TIA (double score), vascular disease, age 65–74 years, sex category (male sex), hyperlipidaemia, smoking, and family history of CAD.

The study was conducted according to the recommendations of the Declaration of Helsinki on Biomedical Research Involving Human Subjects. The Institutional Ethics Committee approved the study protocol, and each participant provided written, informed consent.

Statistical analysis

All analyses were performed using SPSS for Windows (version 18.0, SPSS, Chicago, Illinois). Quantitative variables were expressed as mean value ± standard deviation for parametric variables and median and 25–75 percentile levels for nonparametric variables. Continuous variables were analysed for normal distribution using the Kolmogorov-Smirnov test. Comparisons of parametric values among the SxS groups were performed by one-way analysis of variance. Comparisons of nonparametric values among groups were performed by the Kruskal-Wallis test. The Least Significant Difference (for parametric variables) and Bonferroni adjustment Mann-Whitney U test (for nonparametric variables) were used as a post hoc test for multiple comparisons between the groups. A two-tailed $p < 0.05$ was considered significant. Differences in continuous variables between two groups were determined by student t test or Mann-Whitney U test. The Pearson test was used for correlation of parametric variables and the Spearman test was used to test for nonparametric variables. Logistic regression analysis with the backward method was performed for multivariate analysis of independent predictors. The parameters that had significant $p < 0.05$ were entered in the multivariate analysis.

RESULTS

A total of 454 patients were included in this study. The baseline characteristics and laboratory measurements of patients classified according to SxS tertiles are compared in Table 2. The mean age of patients in the high SxS tertile was significantly higher than that in the intermediate and low SxS tertiles. The prevalence of family history of CAD was higher in the intermediate SxS group than in the other tertiles. The LVEFs were significantly lower in patients with high SxS compared to the intermediate and low SxS tertiles. Patients in the intermediate tertile had significantly higher serum glucose levels compared to the other groups. Serum creatinine levels were significantly lower in the high SxS group compared to the low and intermediate groups. The $CHADS_2$, CHA_2DS_2-VASc, and CHA_2DS_2-VASc-HSF scores were found to be significantly different among the SxS groups.

The $CHADS_2$, CHA_2DS_2-VASc, and CHA_2DS_2-VASc-HSF scores of patients according to SxS groups are listed in Table 3. The SYNTAX score was significantly high in the $CHADS_2 \geq 2$ and CHA_2DS_2-VASc-HSF ≥ 4 groups.

SYNTAX score was weakly correlated with $CHADS_2$, CHA_2DS_2-VASc, and CHA_2DS_2-VASc-HSF scores ($r = 0.239$, $p < 0.001$; $r = 0.218$, $p < 0.001$; $r = 0.271$, $p < 0.001$, respectively) (Fig. 1).

The parameters in which the univariate analysis had p values < 0.05 were entered in the multivariate analysis (age, LVEF, creatinine, glucose, triglycerides, family history of CAD, $CHADS_2$, CHA_2DS_2-VASc, and CHA_2DS_2-VASc-HSF). After multivariate analysis, the CHA_2DS_2-VASc-HSF score was associated with high SxS together with age and LVEF (Table 4).

DISCUSSION

The major finding of the present study is that the newly defined CHA_2DS_2-VASc-HSF score was independently associated with the severity of atherosclerosis in patients with STEMI.

STEMI is an important cause of morbidity and mortality in CAD [10]. Severity of CAD is one of the best predictors of adverse outcome and mortality in STEMI patients [11]. In this study, the burden of atherosclerosis was evaluated by SxS. The SxS is an anatomic scoring system and indicates the characteristics of a lesion including complexity, morphology, and location in the coronary tree. In recent studies it has been reported that high SxS is associated with clinical outcomes including mortality, mortality/reinfarction, major adverse cardiac events, any stent thrombosis at one-year follow-up and long term cardiac mortality (42 months follow-up) in patients with STEMI undergoing primary PCI [11, 12]. The SxS also helps to stratify patients with multivessel and/or left main CAD to either CABG or PCI and reflects the technical difficulty of PCI [11].

The $CHADS_2$ and CHA_2DS_2-VASc scores are clinical predictors used to determine the risk of thromboembolism [1]. These risk scores are widely used in clinical practice and include similar risk factors for the development of CAD. Also, it is known that the factors comprising the CHA_2DS_2-VASc-HSF score promote atherosclerosis and are associated with severity of CAD. Firstly, low ejection fraction is not the cause of complex lesions, but it is the outcome of CAD severity. The number of complex lesions, such as chronic total occlusion, bifurcation and ostial lesions, increase as the SxS increases. Therefore, angiographic lesion characteristics and complexity may impact

Table 2. Baseline characteristics and laboratory measurements of patients classified according to SYNTAX score tertiles

	Low tertile (2–13, n = 151)	SYNTAX score Intermediate tertile (14–20, n = 152)	High tertile (21–40, n = 151)	P
Age [years]	56 ± 12	54 ± 11	61 ± 13	< 0.001$^{\beta\gamma}$
Male gender	118 (78%)	127 (83%)	116 (76%)	0.3
Diabetes mellitus	38 (25%)	29 (19%)	41 (27%)	0.2
Hypertension	55 (36%)	56 (36%)	63 (41%)	0.6
Family history	40 (26%)	63 (41%)	45 (29%)	0.01$^{\alpha}$
Hyperlipidaemia	49 (32%)	32 (21%)	42 (27%)	0.08
Smoking	62 (41%)	79 (52%)	75 (49%)	0.1
CVD	0 (0%)	3 (2%)	5 (3%)	0.1
PAD	10 (6%)	15 (10%)	22 (14%)	0.07
SYNTAX score	8 ± 2	16 ± 2	24 ± 3	< 0.001$^{\alpha\beta\gamma}$
Ejection fraction [%]	48 ± 8	44 ± 7	39 ± 8	< 0.001$^{\alpha\beta\gamma}$
Glucose [mg/dL]	111 (96–134)	129 (108–175)	123 (98–166)	0.006$^{\alpha}$
Creatinine [mg/dL]	1.0 (0.9–1.15); 0.25*	0.9 (0.8–1.0); 0.21*	1.0 (0.8–1.2); 0.40*	0.002$^{\alpha\gamma}$
Uric acid [mg/dL]	5.3 ± 1.5	5.4 ± 1.5	5.6 ± 1.7	0.4
WBC [$\times 10^3$/mm^3]	12 (9–14)	12 (10–14)	12 (10–15)	0.8
Haemoglobin [g/dL]	14.3 ± 1.6	14.3 ± 1.6	14.2 ± 2.0	0.6
Total cholesterol [mg/dL]	195 ± 40	201 ± 39	195 ± 44	0.3
LDL-C [mg/dL]	122 ± 35	130 ± 33	127 ± 38	0.1$^{\alpha}$
HDL-C [mg/dL]	40 (35–47)	38 (32–46)	40 (33–49)	0.2
Trygliceride [mg/dL]	150 (101–211)	132 (82–212)	114 (78–176)	0.03$^{\beta}$
$CHADS_2$	0.90 ± 0.7	0.98 ± 0.9	1.5 ± 1.2	< 0.001$^{\beta\gamma}$
$CHADS_2$-VASc	2.35 ± 1.0	2.31 ± 1.2	3.1 ± 1.6	< 0.001$^{\beta\gamma}$
$CHADS_2$-VASc-HSF	3.90 ± 1.0	4.11 ± 1.1	4.72 ± 1.2	< 0.001$^{\beta\gamma}$

*Interquartile range; $^{\alpha}$Comparison between low SYNTAX score tertile and intermediate SYNTAX score tertile; $^{\beta}$Comparison between low SYNTAX score tertile and high SYNTAX score tertile; $^{\gamma}$Comparison between intermediate SYNTAX score tertile and high SYNTAX score tertile; CVD — cerebrovascular disease; PAD — peripheral artery disease; WBC — white blood cell; LDL-C — low-density lipoprotein-cholesterol; HDL-C — high--density lipoprotein-cholesterol

Table 3. Association of SYNTAX score according to scores

	$CHADS_2$ < 2	$CHADS_2$ ≥ 2	P
SYNTAX score	15.5 (2–40)	19.5 (3–37)	< 0.001
	$CHADS_2$-VASc < 2	$CHADS_2$-VASc ≥ 2	P
SYNTAX score	16.0 (2–40)	17.0 (3–37)	0.05
	$CHADS_2$-VASc-HSF < 4	$CHADS_2$-VASc-HSF ≥ 4	P
SYNTAX score	15.5 (2–30.5)	17.5 (3–40)	< 0.001

ventricular systolic functions. Also, heart failure is associated with neurohumoral and inflammatory parameters due to the relation between inflammation and burden of atherosclerosis. High levels of inflammatory markers, especially high sensitive C-reactive protein, have been associated with left ventricular systolic dysfunction [13].

The other factors comprising the CHA_2DS_2-VASc-HSF, such as HT, age, DM, male gender, hyperlipidaemia, smoking, and family history of CAD, are traditional risk factors for CAD [14, 15]. Moreover, diabetic patients are known to have increased severity of atherosclerosis as well as higher rates for multivessel disease and more complex lesions such

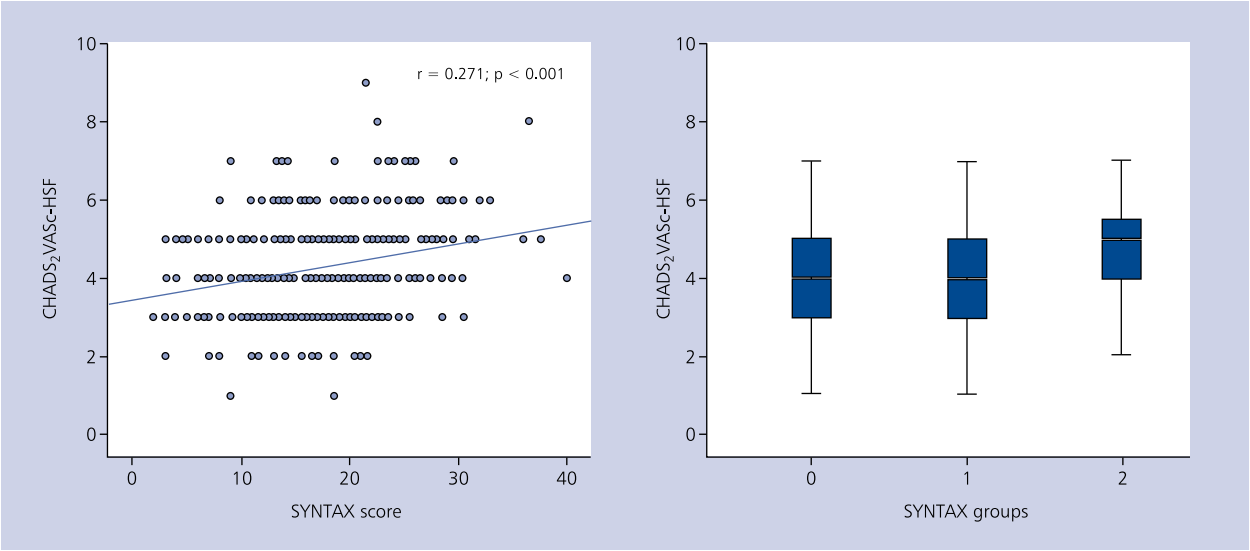

Figure 1. The correlation between $CHADS_2$-VASc-HSF and SYNTAX score; SYNTAX Group 0 — low tertile group; SYNTAX Group 1 — intermediate tertile group; SYNTAX Group 2 — high tertile group

Table 4. Predictors of high SYNTAX score tertile (> 20) in multivariate analyses

	Multivariate odds ratio	95% confidence interval	P
Age	1.032	1.013–1.050	0.001
Family history	1.160	0.646–2.081	0.619
Left ventricular ejection fraction	0.927	0.901–0.955	< 0.001
Creatinine	1.210	0.541–2.708	0.643
Glucose	1.000	0.997–1.003	0.971
Triglycerides	0.999	0.996–1.001	0.237
$CHADS_2$	0.890	0.450–1.760	0.737
$CHADS_2$-VASc	1.014	0.622–1.652	0.957
$CHADS_2$-VASc-HSF	1.258	1.026–1.544	0.028

as long lesions, bifurcation lesions, and diffuse small vessel disease [16, 17]. Furthermore, several studies have demonstrated that HT, smoking, and dyslipidaemia are associated with the complexity of atherosclerosis [18–20]. Also, Sunman et al. [21] indicated that age, male gender, dyslipidaemia, and especially family history of premature CAD were associated with severity and extent of non-calcified coronary atherosclerotic plaques as shown by multidetector computed tomographic coronary angiography. Additionally, in a recent study, investigators suggested that a substantial portion of stroke patients had preclinical CAD and there was a clear association between coronary and cerebral artery atherosclerosis in terms of location and burden [22]. The risk of CAD was particularly high in stroke patients with multiple risk factors and atherosclerosis of the carotid and/or vertebrobasilar arteries [23, 24]. In another study, Korkmaz et al. [25] found increased CAD complexity among patients with acute coronary syndrome and peripheral artery disease, and there was a strong correlation between degree of peripheral artery disease and severity of coronary atherosclerosis [25]. In the present study, CHA_2DS_2-VASc-HSF was associated with the severity of CAD as assessed by SxS.

There are more risk predictors that can affect the severity of atherosclerosis such as biochemical parameters (creatinine, lipoprotein a, homocysteine, high sensitivity C-reactive protein) and echocardiographic parameters (coronary flow reserve, flow mediated dilation, carotid intima–media thickness, aortic stiffness, aortic distensibility). This risk scores can be developed with other parameters in further studies.

Limitations of the study

We had no follow-up data such as in hospital or 30-day mortality and complications that could provide more information on prognostic value of CHA_2DS_2-VASc-HSF score. Also, this

new score should be validated in other MI populations. The CHA_2DS_2-VASc-HSF score can be developed with other biochemical and echocardiographic predictors of atherosclerosis in further studies.

CONCLUSIONS

Traditional risk factors for CAD are associated with severity of atherosclerosis when investigated separately. The purpose of this study was to create an easily remembered formula that includes multiple risk factors, which is associated with the severity of CAD in patients with STEMI. The formula is practical, simple, and useful.

Conflict of interest: *none declared*

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Wartość prognostyczna nowo zdefiniowanej skali CHA_2DS_2-VASc-HSF w ocenie stopnia ciężkości choroby wieńcowej u chorych z zawałem serca z uniesieniem odcinka ST

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Streszczenie

Wstęp: Skale $CHADS_2$ i CHA_2DS_2-VASc są powszechnie stosowane w praktyce klinicznej. Uwzględniają one podobne czynniki ryzyka rozwoju choroby wieńcowej (CAD). Wiadomo, że czynniki zawarte w nowo zdefiniowanej skali CHA_2DS_2-VASc-HSF sprzyjają rozwojowi miażdżycy i wiążą się ze stopniem ciężkości CAD.

Cel: Celem pracy było zbadanie związków między oceną w skali CHA_2DS_2-VASc-HSF a stopniem ciężkości CAD określonym za pomocą skali SYNTAX (SxS) u chorych z zawałem serca z uniesieniem odcinka ST (STEMI).

Metody: Do badania włączono 454 kolejnych chorych z STEMI (mężczyźni 79%, średnia wieku 57,3 ± 12,9 roku) poddanych pierwotnej przezskórnej interwencji wieńcowej. Pacjentów podzielono na trzy grupy w zależności od tercyla punktacji w skali SxS: grupa z niską punktacją w skali SxS (SxS < 14; 151 chorych), grupa z pośrednią punktacją w skali SxS (SxS 14–20; 152 chorych) i grupa z wysoką punktacją w skali SxS (SxS ≥ 21; 151 chorych).

Wyniki: Stwierdzono, że między grupami SxS występowały istotne różnice w punktacji w skalach $CHADS_2$, CHA_2DS_2-VASc i CHA_2DS_2VASc-HSF ($p < 0,001$; $p < 0,001$ i $p < 0,001$). Po przeprowadzeniu analizy wieloczynnikowej punktacja w skali CHA_2DS_2-VASc-HSF wiązała się z wysokim wskaźnikiem SxS (iloraz szans [OR] 1,258; 95% przedział ufności [CI] 1,026–1,544; $p = 0,028$) oraz z wiekiem (OR 1,032, 95% CI 1,013–1,050; $p = 0,001$) i frakcją wyrzutową (OR 0,927; 95% CI 0,901–0,955; $p < 0,001$).

Wnioski: Nowo zdefiniowana skala CHA_2DS_2-VASc-HSF umożliwia ocenę stopnia ciężkości zmian miażdżycowych u chorych z STEMI.

Słowa kluczowe: skala $CHADS_2$-VASc-HSF, stopień ciężkości, choroba wieńcowa, STEMI

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