# **ORIGINAL ARTICLE**

# CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc scores have predictive value in patients with acute coronary syndromes

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## KEY WORDS

#### ABSTRACT

acute coronary syndrome, CHA<sub>2</sub>DS<sub>2</sub>-VASc score, myocardial infarction, prognosis, risk score

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**INTRODUCTION** The CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring systems were designed to stratify thromboembolic risk in patients with atrial fibrillation. The R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score, compared with the CHA<sub>2</sub>DS<sub>2</sub>-VASc, was modified by adding reduced creatinine clearance.

**OBJECTIVES** The aim of the study was to assess the long-term predictive value of these scores in patients with acute coronary syndrome (ACS) and to compare their utility with TIMI and GRACE scores in this patient group.

**PATIENTS AND METHODS** We performed a pooled analysis of 5 independent populations with ACS with a long-term follow-up available. The primary endpoint was defined as all-cause mortality. The following risk scores were calculated: TIMI-STEMI or TIMI-NSTEMI, GRACE,  $CHA_2DS_2$ -VASc, and  $R_2CHA_2DS_2$ -VASc. **RESULTS** A total of 2557 patients were included in the final analysis with a median follow-up of about 5 years. The  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores were significant predictors of total mortality in the pooled analysis. After correction for heart rate and systolic blood pressure on admission as well as previous myocardial infarction, the scores were still significantly predictive of mortality (hazard ratio [HR], 1.47; 95% confidence interval [CI], 1.39–1.54; P < 0.0001 for  $CHA_2DS_2$ -VASc; and HR, 1.41; 95% CI, 1.35–1.47; P < 0.0001 for  $R_2CHA_2DS_2$ -VASc). At all time points (1, 3, and 5 years), the TIMI-STEMI score was a significantly better predictor than the  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores. The predictive value of the  $R_2CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores are significant predictors of all-cause mortality in a long-term follow-up in patients with ACS. These simple risk scores may be easily applied in clinical practice in this patient group.

**INTRODUCTION** The CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were developed to stratify thromboembolic risk in patients with atrial fibrillation (AF).<sup>1</sup> It occurred later that those scales affect all-cause mortality after stroke (in patients with or without AF) or predict the risk of stroke and death in patients who undergo coronary angiography.<sup>2,3</sup> In patients with acute coronary syndrome (ACS), the CHADS<sub>2</sub> score had a strong prognostic value (regardless of whether the patient had AF) in predicting stroke

and mortality, and even greater prognostic value in patients who did not have AF.<sup>4</sup> Recently, a novel score has been developed, R<sub>2</sub>CHADS<sub>2</sub>, modified by adding the kidney disease component and validated in patients with AF as a predictive model of stroke and systemic embolism.<sup>5</sup> Similarly, the modified R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score has shown good calibration and high discriminative performance in the prediction of ischemic stroke and all-cause mortality in patients after myocardial

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infarction.<sup>6</sup> In those publications, ST-segmentelevation myocardial infarction (STEMI) was a minority, and a relatively small proportion of patients were treated invasively.

The aim of the study was to assess the longterm predictive value of the  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores ( $CHA_2DS_2$ -VASc modified by adding reduced creatinine clearance) in ACS patients (mainly with STEMI, treated invasively) and to compare them with the commonly used TIMI and GRACE scores.

PATIENTS AND METHODS Study population We conducted a retrospective registry study of ACS patients hospitalized between 2001 and 2012 in 2 academic cardiology centers in Poland. The clinical data were pooled from 5 independent cardiac registries with long-term follow-up. All but 1 registry comprised unselected consecutive patients with ACS (the Bialystok STEMI genetic registry did not include patients who died within the first 48 hours of hospitalization), in particular: 1) the Warsaw ACS genetic registry enrolled patients with STEMI or non-STEMI [NSTEMI] / unstable angina [UA] hospitalized in the years 2008-2010 (STEMI patients were described by Szpakowicz et al.<sup>7,8</sup>; 2) the Warsaw ACS registry enrolled patients with STEMI or NSTEMI/UA hospitalized in the years 2001–20039; 3) the Bialystok STEMI genetic registry enrolled patients with STEMI hospitalized in the years 2001-2005, who were treated invasively and survived the first 48 hours from hospital admission (described in part by Szpakowicz et al.)<sup>7,8</sup>; 4) the Bialystok STEMI registry, which enrolled patients with STEMI in the years 2000-2002<sup>10,11</sup>; and 5) the Bialystok NSTEMI registry, which enrolled patients with NSTEMI in the years 2009-2012.

The exclusion criteria in all registries were as follows: the final diagnosis other than ACS, age below 18 years, and lack of informed consent. Patients were treated according to the local hospital protocol, which was based on the European Society of Cardiology guidelines. The STEMI protocol involved primary percutaneous coronary intervention as a default treatment strategy. The NSTEMI/UA cohort was stratified according to the GRACE risk score and diagnosed invasively within 2, 24, or 72 hours. Patients were admitted to an invasive cardiac care unit for the first couple of days, and subsequently they were moved to a general cardiology unit and discharged within a week. All demographic and clinical data were entered into the registry for a subsequent evaluation and analysis. Glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease formula.<sup>12</sup> The study protocol was approved by the Ethics Committees of the Medical University of Bialystok and Medical University of Warsaw. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed written consent was obtained from all subjects before their inclusion in the study.

**Follow-up** The long-term follow-up included all-cause mortality. The survival data were obtained according to the personal identification numbers from the Government Central Statistical Office (CSO, PESEL database). Foreigners who did not possess a PESEL (Polish national identification number) were excluded from the analysis.

Risk scores Based on the clinical and demographic characteristics, we retrospectively calculated 5 risk scores for each patient in the registry (with the exception of the Warsaw ACS registry, where TIMI-STEMI and TIMI-NSTEMI were calculated prospectively). These included TIMI-STEMI or TIMI-NSTEMI (when applicable), GRACE, CHA<sub>2</sub>DS<sub>2</sub>-VASc, and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc—a modified CHA<sub>2</sub>DS<sub>2</sub>-VASc score that includes additional 2 points for renal insufficiency (calculated GFR ≤60 ml/kg/min).<sup>5</sup> The CHA<sub>2</sub>DS<sub>2</sub>-VASc, and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were calculated based on hospitalization data and all patients had 1 point in these scores for vascular disease (ACS at the time of inclusion). Any missing data were omitted (cases with missing data were excluded).

**Definitions** In all registries, ACS was defined as severe chest pain lasting more than 15 minutes and not responding to nitroglycerine, also associated with dyspnea, faintness or syncope, as defined by the applicable version of the European Society of Cardiology Guidelines on acute myocardial infarction in patients presenting with persistent ST-segment elevation or without persistent ST-segment elevation of ST-segment or newly diagnosed left bundle branch block on an electrocardiogram and an increase in myocardial necrosis markers.

**Statistical analysis** Medians with interquartile ranges and proportions were used to present the baseline clinical and demographic characteristics. We assessed the adequacy of all risk scores by investigating the area under the curve (AUC) in the receiver-operating characteristics (ROC) analysis. To compare AUCs, the mathematical equivalence to the Mann-Whitney test was used.<sup>19</sup> Kaplan-Meier survival curves were used to depict the difference in survival between the risk subgroups over time. Uni- and multivariate Cox regression analyses were performed to test the predictive value of the risk scores. In the multivariate Cox regression analysis, we used components of the GRACE score that were not replicated in the R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score: heart rate on admission, systolic blood pressure on admission, and previous myocardial infarction. We also performed an analysis with the addition of left ventricular ejection fraction (as a strong independent predictor of mortality), although it could not by applied to the population no. 2 because the ejection fraction was not available in that registry. Two-tailed tests were used, and a P value of less than 0.05 was considered statistically significant.

# TABLE 1 General characteristics of the patients

Variable	Total (n = 2557)	Group 1 (n = 464)	Group 2 (n = 867)	Group 3 (n = 637)	Group 4 (n = 483)	Group 5 (n = 106)
age, y	63 (53–72)	64 (56–74)	63 (52–72)	63 (53–72)	60 (50–67)	69 (59–78)
male sex	1826 (71.6)	341 (73.5)	570 (65.7)	477 (74.9)	364 (75.3)	67 (63.2)
hypertension	1437 (56.2)	313 (67.4)	503 (58.0)	(347 (54.5)	201 (41.6)	73 (68.9)
diabetes	484 (18.9)	98 (21.0)	139 (16.0)	143 (22.4)	76 (15.7)	28 (26.4)
previous myocardial infarction	468 (18.3)	104 (222.4)	228 (26.3)	72 (11.3)	50 (10.4)	14 (13.2)
STEMI	2003 (78.6)	318 (68.5)	565 (65.1)	637 (100)	483 (100)	0 (0)
treatment with primary PCI	2145 (83.9)	416 (89.5)	589 (67.9)	595 (93.4)	479 (99.2)	66 (62.3)
ejection fraction, %	46 (40–52)	47 (40–53)	NA	48 (40–53)	45 (38–50)	48 (38–55)
chronic kidney disease	554 (21.7)	101 (21.8)	217 (25.0)	113 (17.7)	95 (19.7)	28 (26.4)
CHA <sub>2</sub> DS <sub>2</sub> -VASc	3 (2–4)	3 (2–4)	3 (2–4)	3 (2–4)	2 (2–3)	4 (3–5)
R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> -VASc	3 (2–4)	3 (2–5)	3 (2–4)	3 (2–4)	3 (2–4)	4 (3–6)
GRACE	112 (88–135)	100 (81–124)	134 (113–159)	98 (75–118)	97 (75–117)	124 (102–153)
TIMI STEMI	3 (2–5)	3 (1–5)	3 (2–5)	3 (1–4)	4 (2–5)	_
TIMI NSTEMI	3(2–4)	2 (1–4)	3(2–4)	_	_	3 (2–4)

Data are presented as median (interquartile range) or number (percentage) of patients.

CHA<sub>2</sub>DS<sub>2</sub>-VASc, R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc, GRACE, TIMI-STEMI, TIMI-NSTEMI: scores tested in the study (see the Patients and Methods section).

For description of the patient groups, see the Patients and Methods section.

Abbreviations: NA, not available; PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation myocardial infarction

Statistical analyses were done using the SAS software, version 9.2 (Cary, United States).

**RESULTS** We report pooled results of 5 independent populations of patients with myocardial infarction. A total of 2736 patients were initially included in all registries with a median follow-up of 1826 days (about 5 years). Sixteen patients (0.6%) were lost to follow-up, and 163 patients (6.0%) were excluded owing to missing data. The final analysis comprised 2557 patients (mortality rate, 245 patients [9.6%]), a follow-up with a cut-off point of 3 years was available in 2465 patients (mortality rate, 409 patients [16.6%]), and after 5 years, the follow-up was available in 2043 patients (mortality rate, 430 patients [21.0%]). The general characteristics of the study population are shown in TABLE 1. A median value of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 3 (range, 2–4), and of R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score—3 (range, 2–4). The distribution of the risk profile in the study group was as follows: a CHA<sub>2</sub>DS<sub>2</sub>-VASc of 1, 405 patients (15.8%); 2, 731 (28.6%); 3, 612 (23.9%); 4, 429 (16.8%); 5, 242 (9.5%); 6, 101 (3.9%); 7 and more 37 (1.4%); R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc of 1, 363 patients (14.2%); 2, 629 (24.6%); 3, 542 (21.2%); 4, 401 (15.7%); 5, 255 (10.0%); 6, 182 (7.1%); 7, 109 (4.3%); 8 and more 76 (3%).

The CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were strongly significant predictors of total mortality in the pooled analysis (Cox regression model: hazard ratio [HR], 1.46; 95% confidence interval [CI], 1.39–1.53; P <0.0001; and HR, 1.41; 95% CI, 1.36–1.47; P <0.0001; respectively). After correction for heart rate on admission, systolic blood pressure on admission, and previous myocardial infarction, the scores were still significant predictors of mortality (HR, 1.47; 95% CI 1.39–1.54; P < 0.0001 for CHA<sub>2</sub>DS<sub>2</sub>-VASc and HR, 1.41; 95% CI, 1.35–1.47; P < 0.0001 for R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc). Additional correction for left ventricular ejection fraction (on top of the 3 previous factors) did not change the final result. The Kaplan–Meier curves showed a gradually worsening prognosis as the R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score increased (FIGURE 1).

To compare the  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores with GRACE, TIMI-STEMI, and TIMI-NSTEMI scores (all widely used in myocardial infarction), we performed analyses with cutoff points of 1, 3, and 5 years. The *c*-statistics for all scores at all time points are shown in TABLE 2. At all time points, the TIMI-STEMI score performed significantly better than the  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores. The GRACE score was significantly better than the  $CHA_2DS_2$ -VASc score, but compared with  $R_2CHA_2DS_2$ -VASc, the difference was significant only at 1-year follow-up. TIMI-NSTEMI was not different from the  $CHA_2DS_2$ -VASc score and was worse than the  $R_2CHA_2DS_2$ -VASc score (TABLE 3).

The *c*-statistics for the GRACE score for NSTEMI patients was significantly better than the  $CHA_2DS_2$ -VASc score at all time points and comparable with the  $R_2CHA_2DS_2$ -VASc score. In STEMI patients, the GRACE score was better than the  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores at all time points, but the difference after 5 years was not significant with the  $R_2CHA_2DS_2$ -VASc score (TABLE 2).

The R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score presented better predictive values than the CHA<sub>2</sub>DS<sub>2</sub>-VASc score

FIGURE 1 Kaplan– –Meier curves showing prognosis depending on grouped  $R_2CHA_2DS_2$ -VASc scores (1 and 2 vs 3 and 4 vs >5). Time scale is shown in davs.



### TABLE 2 C-statistics for the scores

	Follow-up				
Score	1-year	3-year	5-year		
CHA2DS2-VASc	0.675	0.694	0.688		
R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.725	0.721	0.711		
GRACE	0.780	0.746	0.732		
TIMI STEMI	0.794	0.765	0.753		
TIMI NSTEMI	0.622	0.649	0.644		
CHA2DS2-VASca	0.670	0.687	0.698		
R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> -VASc <sup>a</sup>	0.737	0.744	0.765		
<b>GRACE</b> <sup>a</sup>	0.735	0.742	0.735		
CHA2DS2-VAScb	0.671	0.693	0.686		
R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> -VASc <sup>b</sup>	0.717	0.713	0.701		
<b>GRACE</b> <sup>b</sup>	0.794	0.760	0.731		

a patients with NSTEMI,

b patients with STEMI

#### Abbreviations: see TABLE 1

after 1, 3, and 5 years of follow-up. At all time points, *c*-statistic values were significantly higher for the  $R_2CHA_2DS_2$ -VASc score (0.725 vs 0.675 [*P* <0.0001], 0.721 vs 0.694 [*P* <0.0001], and 0.711 vs 0.688 [*P* = 0.002], respectively). When  $R_2CHA_2DS_2$ -VASc score components were analyzed separately (Cox regression model), only female sex was not a significant predictor of mortality in long-term follow-up in the univariate analysis. Interestingly, in the multivariate

analysis, hypertension was not a significant predictor of mortality, but female sex had a protective effect. The strongest predictors of mortality were age, chronic kidney disease, and previous stroke (TABLE 4).

**DISCUSSION** We have shown that in patients with ACS the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is a good predictor of long-term mortality. CHA<sub>2</sub>DS<sub>2</sub>-VASc modified by adding renal disease (R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc) had a better predictive value compared with CHA<sub>2</sub>DS<sub>2</sub>-VASc. We introduced and validated the R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score similarly to the RCHADS<sub>2</sub> score based on a ROCKET AF trial subanalysis, which showed that the association between renal function and stroke was independent of, and additive to, the CHADS<sub>2</sub> score.<sup>5</sup>

Furthermore, our results have also shown that CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc were worse predictors than specific ACS scores like TIMI-STEMI and GRACE, at least in the short--term follow-up. The R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score was comparable to the GRACE score in the longterm follow-up (3 and 5 years). Considering that CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc are simple, and at least CHA<sub>2</sub>DS<sub>2</sub>-VASc is a widely known score, we believe that this might be a reasonable alternative to complicated and more specific ACS scores. It should be emphasized that the value of the scores in STEMI patients is limited, and the role of immediate invasive treatment is 
 TABLE 3
 Comparison of c-statistics between the tested scores at different time points

Scores	1 year		3 years		5 years	
	delta (95% CI)	P value	delta (95% CI)	P value	delta (95% CI)	P value
GRACE vs CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.105 (0.069–0.142)	< 0.001	0.052 (0.023–0.082)	< 0.001	0.044 (0.012–0.076)	0.007
GRACE vs R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.056 (0.017–0.23)	0.001	0.025 (-0.002–0.053)	0.07	0.020 (-0.009–0.050)	0.2
TIMI STEMI vs CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.122 (0.078–0.166)	< 0.001	0.067 (0.033–0.100)	< 0.001	0.064 (0.031–0.096)	< 0.001
TIMI STEMI vs R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> VASc	0.077 (0.038–0.116)	< 0.001	0.047 (0.016–0.078)	0.003	0.048 (0.017–0.079)	0.003
TIMI NSTEMI vs CHA <sub>2</sub> DS <sub>2</sub> - -VASc	-0.048 (-0.134-0.038)	0.3	-0.027 (-0.100-0.046)	0.5	-0.047 (-0.129-0.034)	0.3
TIMI NSTEMI vs R <sub>2</sub> CHA <sub>2</sub> DS <sub>2</sub> - -VASc	-0.116 (-0.206 to -0.025)	0.01	–0.083 (–0.159 to –0.007)	0.03	-0.115 (-0.192 to -0.038)	0.004

Abbreviations: CI, confidence interval; others, see TABLE 1

TABLE 4 Effect of individual R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc components on mortality

Parameter	Univariate analysis			Multivariate analysis				
	HR	95% CI	P value		HR	95% CI	P value	
heart failure	1.86	1.57–2.22	< 0.0001		1.41	1.18–1.70	0.0003	
hypertension	1.28	1.08–1.51	0.0036		0.98	0.82-1.18	0.83	
diabetes	1.81	1.51–2.16	< 0.0001		1.50	1.24–1.83	< 0.0001	
age ≥65 years	3.13	2.62-3.72	< 0.0001		1.99	1.60-2.49	< 0.0001	
stroke	2.42	1.76–3.33	< 0.0001		1.83	1.32–2.54	0.0003	
vascular disease	1.88	1.57–2.26	< 0.0001		1.46	1.21–1.77	< 0.0001	
age ≥75 years	3.43	2.90-4.05	< 0.0001		2.08	1.70–2.56	< 0.0001	
female sex	0.98	0.82–1.17	0.80		0.67	0.55–0.81	< 0.0001	
chronic kidney disease	2.84	2.40-3.37	< 0.0001		2.00	1.66–2.41	< 0.0001	

Abbreviations: HR, hazard ratio; others, see TABLE 3

unquestionable. On the other hand, in NSTEMI patients, TIMI-NSTEMI and GRACE scores have been validated in prospective analyses; therefore, by now they cannot be replaced by CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc scores.

Our results are not surprising when particular components of CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>--VASc scores are analyzed separately. Such factors as age, diabetes,<sup>20</sup> or a history of heart failure<sup>21</sup> are widely known in the determination of long--term mortality after myocardial infarction. We confirmed the value of those factors and showed that the most potent factors influencing mortality from R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc score are age, chronic kidney disease, and previous stroke. The CHADS<sub>2</sub> score is a good predictor of total mortality in patients with AF, in patients with a history of stroke,<sup>22</sup> and in patients with syncope.<sup>23</sup> In heart failure patients with a cardiac resynchronization therapy defibrillator, the CHA2DS2-VASc score was an independent predictor of major clinical events at 30-month follow-up.24

Recently, Poci et al.<sup>4</sup> have shown that the  $CHADS_2$  score is a good predictor of longterm mortality in patients with ACS, irrespective of the presence of AF in the acute phase.<sup>4</sup> Our results were obtained from more contemporary populations, with a much higher percentage of patients receiving invasive treatment. We present similar results on a different population (although still ACS): in our group about 75% of the patients had STEMI (onethird in a study by Poci et al.<sup>4</sup>) and most of our population was treated invasively (one--third in a study by Poci et al.<sup>4</sup>). Interestingly the *c*-statistics of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score in predicting long-term mortality were comparable in both populations (0.688 vs 0.643 in Poci et al.<sup>4</sup>). Finally, in the cited paper, the GRACE score was significantly better than the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores, and the *c*-statistics for the GRACE score in long-term mortality were comparable with that in our population (0.749 vs 0.732, respectively).

Another publication that validated the CHA<sub>2</sub>-DS<sub>2</sub>-VASc score in patients with myocardial infarction was the paper by Barra et al.<sup>6</sup> Their population was much more up-to-date than that in the study by Poci et al.,<sup>4</sup> but still the percentage of patients with STEMI was much lower compared with our population (42% vs 78%) and the followup was shorter. They showed a very good predictive value of the CHA<sub>2</sub>DS<sub>2</sub>-VASc and R-CHA<sub>2</sub>DS<sub>2</sub>--VASc scores with respect to stroke rate and total mortality (R-CHA<sub>2</sub>DS<sub>2</sub>-VASc score included CHA<sub>2</sub>DS<sub>2</sub>-VASc and renal insufficiency, blood urea nitrogen, presence of AF, and a history of revascularization). A 6-month value of the R-CHA<sub>2</sub>DS<sub>2</sub>--VASc score in predicting mortality was comparable to that of the GRACE score.

It has been also shown that the CHADS<sub>2</sub> score was an independent predictor of future major adverse cardiovascular events (MACEs) including death, nonfatal myocardial infarction, and ischemic stroke. Interestingly, the authors found the CHADS<sub>2</sub> score to be a better predictor of MACEs than TIMI risk scores.<sup>25</sup> On the other hand, in the group of AF patients after PCI (but about 40% of patients with stable angina), the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were significant predictors of MACEs, and only the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was a significant predictor of all-cause mortality. Interestingly, the predictive value of the scores was only modest (*c*-statistics, 0.56–0.57), far lower than we observed for the CHA<sub>2</sub>DS<sub>2</sub>-VASc score.<sup>26</sup>

Limitations Our study has several limitations. The patient data were collected within a 10-year period, so obviously the management of patients in the active phase and during the long-term follow-up has changed. The Bialystok STEMI genetic registry enrolled patients with STEMI who survived the first 48 hours from hospital admission, which decreased the risk in this group. Our groups were well described and the follow-up was made using government data, so only a few patients were missing. A major limitation of the study is total mortality as the only endpoint; however, the GRACE and TIMI risk scores were also developed to assess the risk of all-cause death. In our population, STEMI patients represented the majority, so the results apply primarily to this subgroup; still the value of the scores in contemporary treatment of STEMI patients is limited. Patients with NSTEMI/UA were analyzed together because of the small number of patients. We confirmed the value of the CHA<sub>2</sub>DS<sub>2</sub>-VASc and R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc scores only in long-term follow-up. However, the analysis was retrospective; therefore, the prospective value of the scores is yet to be established.

**Conclusions** The  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores are significant predictors of all-cause mortality in short- and long-term follow-up in patients presenting with ACS. The scores perform worse than the TIMI-STEMI score, but the  $R_2CHA_2DS_2$ -VASc score is comparable to the GRACE score in long-term follow-up. The  $CHA_2DS_2$ -VASc and  $R_2CHA_2DS_2$ -VASc scores are simple and can easily be applied in clinical practice.

**Contribution statement** MK, AS, KJF, WJM, KAK, and GO conceived the idea for the study and contributed to the design of the research. MK, AS, ŁK, DP, FS, MB, and EN were involved in data collection. MP performed statistical analysis. All authors were involved in data interpretation. MK drafted the article. All authors revised the manuscript and approved the final version.

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# **ARTYKUŁ ORYGINALNY**

# Skale CHA<sub>2</sub>DS<sub>2</sub>-VASc i R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc mają wartość prognostyczną u chorych z ostrym zespołem wieńcowym

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### SŁOWA KLUCZOWE

## STRESZCZENIE

ostry zespół wieńcowy, rokowanie, skala CHA<sub>2</sub>DS<sub>2</sub>-VASc, skala ryzyka, zawał serca **WPROWADZENIE** CHA<sub>2</sub>DS<sub>2</sub>-VASc i R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc zostały stworzone w celu oceny ryzyka zakrzepowo--zatorowego u chorych z migotaniem przedsionków. Skala R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc, w porównaniu ze skalą CHA<sub>2</sub>DS<sub>2</sub>-VASc, została zmodyfikowana z uwzględnieniem obniżonego klirensu kreatyniny.

**CELE** Celem badania była ocena wartości prognostycznej powyższych skal w odległej obserwacji chorych z ostrym zespołem wieńcowym (OZW) oraz porównanie ich przydatności w tej grupie chorych z powszechnie używanymi skalami TIMI i GRACE.

PACJENCI I METODY Przeprowadziliśmy łączną sumaryczną analizę 5 niezależnych populacji chorych z OZW z dostępną odległą obserwacją. Pierwotnym punktem końcowym była śmiertelność całkowita w odległej obserwacji. Oceniano następujące skale ryzyka: TIMI-STEMI lub TIMI-NSTEMI, GRACE, CHA<sub>2</sub>DS<sub>2</sub>-VASc oraz R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc.

**WYNIKI** W analizie uwzględniono 2557 pacjentów z medianą obserwacji równą około 5 lat. Skale  $CHA_2DS_2$ -VASc i  $R_2CHA_2DS_2$ -VASc były silnymi i istotnymi predyktorami śmiertelności w całej analizie. Po skorygowaniu o częstotliwość rytmu, ciśnienie skurczowe krwi przy przyjęciu oraz o przebyty zawał serca wynik pozostał istotny statystycznie (HR 1,47; 95% Cl 1,39–1,54; p <0,0001 dla skali CHA\_2DS\_2-VASc oraz HR 1,41; 95% Cl 1,35–1,47; p <0,0001 dla skali R\_2CHA\_2DS\_2-VASc). We wszystkich analizowanych punktach czasowych (1, 3 i 5 lat) skala TIMI-STEMI miała istotnie wyższą wartość prognostyczną niż skale CHA\_2DS\_2-VASc i R\_2CHA\_2DS\_2-VASc. Skala R\_2CHA\_2DS\_2-VASc w obserwacji 3- i 5-letniej miała zbliżoną zdolność predykcyjną do skali GRACE.

**WNIOSKI** Skale CHA<sub>2</sub>DS<sub>2</sub>-VASc i R<sub>2</sub>CHA<sub>2</sub>DS<sub>2</sub>-VASc są istotnymi predyktorami śmiertelności całkowitej w odległej obserwacji chorych z OZW. Te proste narzędzia oceny ryzyka mogą łatwo znaleźć nowe zastosowanie kliniczne w tej grupie chorych.

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