ORIGINAL ARTICLE

The association of acute-to-chronic glycemic ratio with no-reflow in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

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KEY WORDS
acute-to-chronic glycemic ratio, myocardial infarction, no-reflow, percutaneous coronary intervention

ABSTRACT

BACKGROUND No-reflow (NR) is a strong and independent predictor of poor cardiovascular outcomes among patients with ST-segment elevation myocardial infarction (STEMI).

AIMS The aim of the study was to investigate the association of the acute-to-chronic (A/C) glycemic ratio with no-reflow (NR) in STEMI patients following primary percutaneous coronary intervention (PCI).

METHODS This retrospective study included 905 patients with STEMI. The A/C glycemic ratio was determined as admission blood glucose (ABG) divided by the estimated average glucose (eAG). We evaluated 2 primary models (full model and reduced model). The primary outcome was the presence of NR.

RESULTS The incidence of NR was 22.7% (206 cases) in the present study. We divided the study population into 3 tertiles (T1, T2, and T3) based on the ABG/eAG ratio. There was a stepwise increase of the frequency of NR from the T1 to T3 group (36 patients [12%] vs 70 patients [23%] vs 100 patients [33%]; respectively [P <0.001, for each group comparison]). In a full model, the ABG/eAG ratio (OR, 2.274; 95% CI, 1.587–3.26; P <0.001) was associated with NR. After the performance of a step-down backward variable selection method, the thrombus grade, the ABG/eAG ratio, the infarct-related artery diameter, and age remained in the reduced model. The ABG/eAG ratio (contributing 25.3% of the explainable outcome in the model) was one of the strong predictors of NR in the reduced model.

CONCLUSIONS To our knowledge, this might be the first study showing a significant relationship between the ABG/eAG ratios with NR in patients with STEMI after primary PCI.

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INTRODUCTION Although primary percutaneous coronary intervention (PCI) is the best treatment option for patients who present with ST-segment elevation myocardial infarction (STEMI), a sizable proportion of post-PCI patients may not achieve an adequate myocardial perfusion despite the removal of mechanical obstruction in the infarct-related artery.[1] This phenomenon is known as no-reflow (NR). NR is the Achilles heel of primary PCI, and studies show that the occurrence of such an event is a strong and independent predictor of poor cardiovascular outcomes, including acute heart failure, cardiogenic shock, and life-threating arrhythmias among STEMI patients.[2,3] Even though the underlying mechanism of NR is somewhat complex and not well-understood, several pathogenic mechanisms, such as endothelial dysfunction, microvascular impairment, and reperfusion injury, have been shown to be related to the occurrence of this event.[4,5] Recently, clinical

WHAT'S NEW?

Prior studies demonstrated that acute-to-chronic glycemic ratio is an independent predictor of mortality in patients with acute coronary syndrome, including ST-segment elevation myocardial infarction. No-reflow is an unwanted complication of percutaneous coronary intervention, especially in ST-segment elevation myocardial infarction patients. This study tested the predictive value of this index for no-reflow in patients with ST-segment elevation myocardial infarction. Our results revealed that the acute-to-chronic glycemic ratio was significantly associated with no-reflow in this population. To our knowledge, this is the first study showing such a relationship among these patients.

studies have also revealed that admission blood glucose (ABG) and chronic hyperglycemic state are related to an increased risk of NR in patients with STEMI even after successful revascularization with primary PCI.[6,7] Both conditions have been considered to have an adverse effect on platelet and endothelial function as well as causing microvascular dysfunction, thereby resulting in NR.

In STEMI, acute hyperglycemia or ABG is an indicator of stress hyperglycemia that usually occurs due to the abrupt increase of catecholamine levels.[8] However, ABG may not represent the true acute glycemic status because it is also affected by chronic glycemic levels, especially in patients with diabetes. Therefore, a novel index, which is termed the acute-to-chronic (A/C) glycemic ratio or stress hyperglycemia ratio, has been proposed to better show the true acute glycemic rise in patients with acute medical illness.[9] This index is calculated as ABG divided by the estimated average glucose (eAG). In recent studies, it has been found that the use of ABG/eAG ratio has an adequate performance compared with the use of absolute hyperglycemia for predicting poor cardiovascular outcomes, such as cardiogenic shock and acute pulmonary edema, both in nondiabetic and diabetic patients with STEMI.[10,11] However, the data regarding the relation of ABG/eAG ratio with NR in patients with STEMI treated with primary PCI have not yet been explored. Hence, in the current study, we investigate the association of ABG/eAG ratio with NR in STEMI patients following primary PCI.

METHODS

Data collection This was a retrospective and observational study that included patients who were diagnosed with STEMI and treated with primary PCI in a tertiary heart center. All patients were consecutively included during the study period from March 2016 to March 2018. In this analysis, we applied the following exclusion criteria: diagnosed hemoglobinopathy, mechanical complications, a history of an urgent aorta-coronary bypass grafting, and missing clinical data for ABG or glycated hemoglobin A_{1c} (HbA_{1c}). Finally, the study cohort involved 905 consecutive STEMI patients. All of the patients during in-hospital study were treated in accordance with the current STEMI guidelines. Baseline demographic features, including hypertension, diabetes mellitus, hyperlipidemia, and so on as well as laboratory, and angiographic findings were retrieved from our hospital electronic database. All patients in the present study were evaluated at admission using Killip class.

Laboratory analysis In the present study, blood samples including hemoglobin levels, white blood cell counts, platelet counts, and blood glucose levels were measured at admission in all studied patients. Hematologic parameters were measured as part of the automated complete blood count, using the Sysmex XN 9000 hematology analyzers (Sysmex Corporation, Kobe, Japan). Biochemical measurements were performed using Beckman Coulter, Inc. kits and calibrators (Beckman Coulter Life Sciences, Indianapolis, Indiana, United States). The HbA_{1c} level was determined using a high-performance liquid chromatography analyzer. Total cholesterol and low-density lipoprotein cholesterol were determined after 8 to 12 hours of overnight fasting.

Coronary angiography and percutaneous coronary intervention In all of the patients, the standard coronary angiography via the femoral or radial approach was performed using 5- or 6-French Judkins diagnostic catheters (Medtronic, Minneapolis, Minnesota, United States). Patients without contraindications were treated with 300 mg of acetylsalicylic acid along with a loading dose of either 600 mg of clopidogrel or 180 mg of ticagrelor or 60 mg of prasugrel before the coronary angiography. During the coronary intervention, the standard intravenous bolus unfractionated heparin (70–100 U/kg), with additional doses if necessary, was given to achieve an activating clotting time longer than 250 seconds. All coronary angiograms were recorded in digital media for quantitative analysis (DICOM-viewer; MedCom GmbH, Darmstadt, Germany). The stenting of the infarct-related artery with a drug-eluting or bare metal stent was performed immediately after the coronary angiography. Per institutional protocol, the use of glycoprotein IIb/IIIa inhibitor was left at the operator's discretion. Two experienced cardiologists, who were blinded to all clinical data, analyzed the thrombolysis in myocardial infarction (TIMI) flow grade before and after the intervention. In cases of disagreement, the same 2 cardiologists reviewed the coronary angiograms and came to a joint agreement. Thrombi were graded from 1 to 5, where 1 indicates no thrombus and 5 indicates a very large thrombus causing vessel occlusion. Additionally, grade 5 thrombus was reclassified from grade 1 to grade 4 after recanalization with a guide wire or a small balloon. Manual mechanical thrombectomy was not mandatory in the presence of thrombus per

TABLE 1 The baseline characteristics of all patients

Characteristics		ABG / eAG tertiles			
		T1 (≤0.96); n = 305	T2 (0.97–1.16); n = 301	T3 (≥1.17); n = 299	*P* value
Age, y		56 (49–65)	58 (50–67)	57 (50–66)	0.35
Male sex		255 (84)	247 (82)	239 (80)	0.50
Body mass index, kg/m^2		26.8 (24.4–29.4)	27.2 (24.3–29.5)	27.4 (24.4–29.7)	0.50
History					
Hypertension		129 (43)	131 (44)	147 (49)	0.23
DM		83 (27)	78 (26)	135 (45)	<0.001
Family history		91 (30)	87 (29)	86 (29)	0.94
Hyperlipidemia		14 (5)	20 (7)	26 (9)	0.13
Coronary artery disease		70 (230)	57 (19)	46 (15)	0.055
Current smoking status		238 (78)	238 (79)	225 (75)	0.51
CVD		7 (2)	15 (5)	12 (4)	0.21
Chronic kidney disease		9 (3)	6 (2)	14 (5)	0.17
On admission					
SBP, mm Hg		134 (115–155)	135 (115–155)	136 (115–154)	0.95
DBP, mm Hg		77 (70–90)	77 (70–88.5)	78.5 (70–90)	0.81
Killip class	1	295 (97)	292 (98)	276 (93)	0.01
	2	2 (1)	0 (0)	7 (2)	
	3	2 (1)	3 (1)	4 (1)	
	4	4 (1)	3 (1)	11 (4)	
Heart rate, bpm		79 (67–92)	78 (64.5–88)	81 (68–95)	0.02
Nonanterior MI		183 (61)	194 (65)	166 (56)	0.06
History of medical therapy					
Antiplatelet treatment		52 (18)	51 (18)	41 (14)	0.39
β-Blocker		36 (12)	39 (13)	25 (9)	0.15
Statin		26 (9)	19 (7)	16 (5)	0.26
ACE-inhibitor		49 (17)	47 (16)	50 (17)	0.96
Oral antidiabetic		24 (8)	8 (3)	33 (11)	<0.001
Insulin treatment		28 (28.6)	24 (24.5)	46 (46.9)	0.93
Pre-PCI antiplatelet treatment					
Clopidogrel		106 (33)	104 (32.4)	111 (34.6)	0.93
Prasugrel / ticagrelor		199 (34.1)	196 (33.6)	188 (32.2)	

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

Abbreviations: ABG, admission blood glucose; ACE, angiotensin converting enzyme; CVD, cerebrovascular disease; DM, diabetes mellitus; eAG, estimated average glucose; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention

hospital protocol. The SYNTAX scoring system was used to evaluate the severity of coronary artery disease using an online web calculator.

Definitions STEMI is described as proposed in the recent universal definition of myocardial infarction guideline.[12] In the current study, the angiographic NR is described as a TIMI flow grade of less than 3 with the absence of coronary spasm or dissection. As proposed in a previous study, we determined the eAG from HbA_{1c}, and it was calculated using the following equation: eAG (mg/dl) = (28.7 × HbA_{1c}%) – 46.7.[9] The A/C glycemic ratio, in which the ABG was divided by eAG, was estimated in all patients using the first measurement of blood glucose at admission and estimation of chronic glucose levels. The criterion for diabetes mellitus was accepted as having

follow-up fasting blood glucose levels fulfilling the American Diabetes Association's criteria or as taking oral antidiabetics or insulin.[13]

Statistical analysis All statistical analyses were performed using "rms" and "Hmisc" packages with the R software, version 3.5.1 (R Statistical Software, Institute for Statistics and Mathematics, Vienna, Austria). Continuous variables were presented as median and interquartile range (IQR), whereas categorical variables were presented as counts and percentages.

The primary outcome was defined as the presence of NR.

It is important that candidate predictors included in the model are clinically and biologically plausible and that their association with NR has been demonstrated in previous studies. Variables with very low or very high frequency were not included in the model. Also, we did not include any missing variables more than 50% in our model. The candidate predictors were chosen according to these principles.[14] We used adjusted multivariable penalized logistic regression analysis to examine the relationship between primary outcome and candidate predictors. Effects of individual predictors on NR were reported by using odds ratio (OR) and 95% CI. The effects of continuous predictors were summarized using their IQR. We evaluated 2 primary models. The first model included 14 predictor variables (full model). The candidate predictors were age, sex, ABG/eAG ratio, diabetes, smoking, myocardial infarction type, Killip class, systolic blood pressure, infarct-related artery diameter, thrombus grade, hemoglobin, previous statin use, creatinine, and ABG/eAG interaction with diabetes mellitus (ABG/eAG × diabetes mellitus). To decrease the complexity of the full model and to yield reduced-form models that would be more practical for bedside use, we performed step-backward variable selection with an α criterion of 0.25.[14] The comparison between models (full and reduced) was made with assessment of fit (likelihood ratio χ^2), quality (Akaike and Bayesian information criteria), and predictive accuracy (c index), and R^2. The ABG/eAG ratio was included in the model as continuous parameter using a restricted cubic spline with 4 knots. The relative importance of each predictor in the models was estimated with partial χ^2 value for each predictor divided by the model's total χ^2, which estimates the independent contribution of the predictor to the variance of the outcome. Sample size for NR modeling must be sufficiently large or the number of predictor variables must be sufficiently conservative for the model to be reliable and accurate. Specifically, there must be ideally 10 to 20 participants having the primary outcome per candidate predictor variables. Our model had 14 predictors and there were 206 participants who met the need for NR criteria, thus allowing approximately 10 to 20 predictors for this model to avoid overfitting.[14]

Ethical standards All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. The ethics committee approved the design of the present study (no. 2019/KK/158). Informed consent was waived due to the retrospective design of the study.

RESULTS In total, 905 STEMI patients were included in this analysis (median [IQR] age, 57 [50–66] years; 164 patients [18.1%] were female). The incidence of NR was 22.7% (206 cases) in the present study. The median (IQR) value for ABG and the ABG/eAG ratio was 130 (110–176) mg/dl and 1.04 (0.9–1.23) mg/dl, respectively.

We divided the sample size into 3 tertiles (T1, T2, and T3) based on the ABG/eAG ratio. TABLE 1 and TABLE 2 are a presentation of baseline clinical

TABLE 2 Laboratory investigations and angiographic data of all patients (continued on the next page)

Parameter	ABG / eAG tertiles			
	T1 (≤0.96); n = 305	T2 (0.97–1.16); n = 301	T3 (≥1.17); n = 299	*P* value
Laboratory assessment				
HbA_{1c}, %	5.9 (5.6–6.4)	5.8 (5.5–6.4)	5.9 (5.6–7.5)	0.12
ABG, mg/dl	105 (96–117)	127 (116–147)	178 (148.5–276)	<0.001
eAG, mg/dl	122.6 (114–137)	119.8 (111–137)	122.6 (114–168.5)	0.12
ABG/eAG ratio	0.85 (0.78–0.91)	1.05 (1–1.1)	1.35 (1.24–1.56)	<0.001
Hemoglobin, g/dl	13.9 (12.7–15)	13.7 (12.6–14.9)	14.2 (12.9–15.2)	0.16
WBC count, cells/μl	11.5 (9.2–13.8)	11.6 (9.4–13.7)	11.8 (9.8–14.7)	0.08
Platelet count, cells/μl	237 (197–277.2)	225 (193–269)	234 (196–282.5)	0.52

TABLE 2 Laboratory investigations and angiographic data of all patients (continued from the previous page)

Parameter		ABG / eAG tertiles			
		T1 (≤0.96); n = 305	T2 (0.97–1.16); n = 301	T3 (≥1.17); n = 299	*P* value
Laboratory assessment					
Peak troponin I, ng/dl		24 (9–46.7)	31.6 (14.2–50)	31.3 (8.6–49)	0.056
Peak CK-MB, ng/ml		77.7 (38.9–161)	103.3 (41.6–195)	96.6 (47.1–224)	0.04
Total cholesterol, mg/dl		183.5 (160–211)	173.5 (144–202)	172 (148–203.7)	0.004
LDL cholesterol, mg/dl		116 (94–142)	106 (84–134)	107 (86–130)	0.003
Angiographic parameters					
Door to balloon time, min		70 (30–150)	90 (30–150)	75 (30–150)	0.56
Pain to balloon time, min		90 (30–240)	90 (40–180)	65 (30–180)	0.15
Total ischemia time, min		150 (90–420)	180 (120–390)	180 (90–390)	0.34
Diseased vessel					
Number of diseased vessels	1	168 (55)	175 (58.1)	165 (55.1)	0.58
	2	88 (29)	89 (30)	92 (31)	
	3	49 (16)	37 (12.6)	42 (14)	
Syntax score		13 (8–20)	14 (8–20)	16.5 (10–22.5)	<0.001
Residual Syntax score		2 (0–9)	3 (0–10)	5 (0–10)	0.15
IRA					
Diameter, mm		3 (2.75–3)	3 (2.75–3)	3 (2.75–3.5)	0.11
DES implantation		220 (85)	214 (85)	206 (80)	0.95
Stent length, mm		22 (16–28)	22 (15–28)	22 (16–28)	0.53
Predilation		235 (77)	235 (78)	233 (78)	0.95
Postdilation		79 (26)	77 (26)	86 (29)	0.63
Pre-TIMI					
0		208 (68)	223 (74)	232 (78)	0.005
1		44 (14)	51 (17)	39 (13)	
2		53 (17)	27 (9)	28 (9)	
Post-TIMI					
0		18 (6)	14 (5)	17 (6)	<0.001
1		14 (5)	15 (5)	25 (8)	
2		4 (1)	41 (14)	58 (19)	
3		269 (88)	231 (77)	199 (67)	
Thrombus grade					
0		64 (21)	60 (20)	59 (20)	0.55
1		85 (28)	91 (30)	92 (31)	
2		29 (10)	36 (12)	23 (8)	
3		53 (17)	42 (14)	52 (17)	
4		65 (21)	65 (22)	58 (19)	
5		9 (3)	7 (2)	15 (5)	
No-reflow					
Patients		36 (12)	70 (23)	100 (33)	<0.001

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

Abbreviations: CK-MB, creatinine kinase-myocardial band; DES, drug-eluting stent; IRA, infarct-related artery; LDL, low-density lipoprotein; TIMI, Thrombolysis In Myocardial Infarction; WBC, white blood cell; others, see TABLE 1

TABLE 3 Adjusted multivariable penalized logistic regression analysis for candidate predictors of no-reflow

Variable	Odds ratio	95% CI	*P* value
ABG/eAG ratio	2.274	1.587–3.26	<0.001
Age	1.552	1.189–2.025	0.0012
Killip class	1.499	0.527–4.268	0.45
Systolic blood pressure	0.922	0.718–1.183	0.52
IRA diameter	0.844	0.766–0.930	<0.001
Thrombus grade	1.869	1.457–2.399	<0.001
Hemoglobin	1.089	0.847–1.400	0.0504
Creatinine	1.078	0.997–1.165	0.0059
Diabetes mellitus	1.634	1.087–2.456	0.06
Male sex	0.932	0.561–1.548	0.78
Smoking	1.007	0.634–1.602	0.97
Nonanterior MI location	1.371	0.958–1.963	0.09
Statin use	1.085	0.561–2.098	0.81
ABG/eAG × DM[a]	–	–	0.83

a Interaction between the admission blood glucose to estimated average glucose ratio and diabetes mellitus

Abbreviations: see TABLES 1 and 2

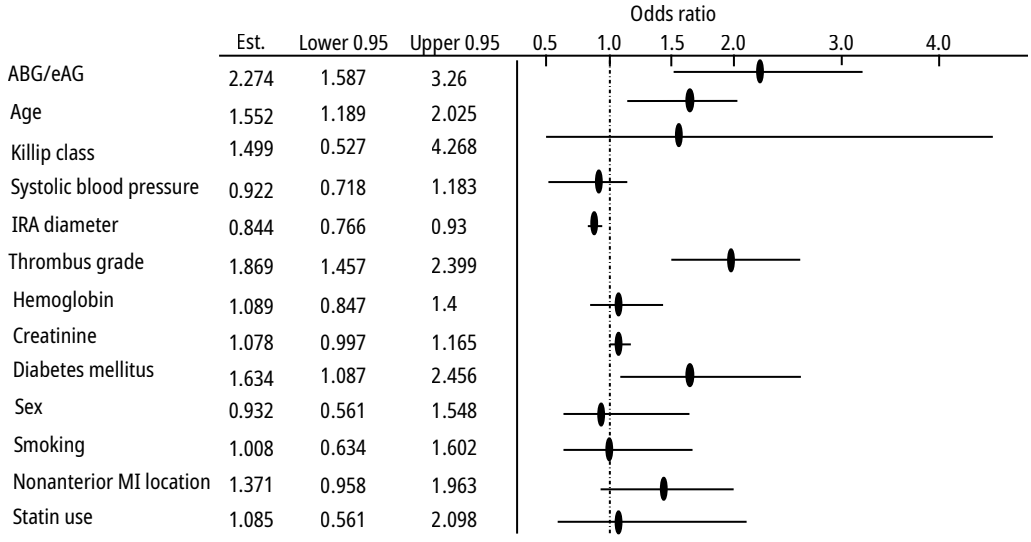

FIGURE 1 The candidate predictors of no-reflow that were included in the full model

Abbreviations: DM, diabetes mellitus; others, see TABLES 1 and 2

features, laboratory, and angiographic findings for all patients. The frequency of diabetes mellitus was higher in patients allocated into the T3 group (*P* <0.001). The other baseline demographic features were similar across the groups. While patients' systolic and diastolic blood pressure and the location of myocardial infarction were indifferent across the groups, patients in the T3 group had higher Killip class scores and heart rate on admission. We did not observe any differences regarding insulin therapy or pre-PCI antiplatelet treatment, including clopidogrel, ticagrelor or prasugrel, between the tertiles. In terms of laboratory investigations, ABG, ABG/eAG ratio, peak creatinine kinase-myocardial band levels, and creatinine levels were higher in patients allocated into the T3 group. Comparison of angiographic parameters revealed that patients in the T3 group had a higher SYNTAX score, pre- and post-TIMI flow. There was a stepwise increase of the frequency of NR from the T1 to T3 group (36 patients [12%] vs 70 patients [23%] vs 100 patients [33%], respectively; *P* <0.001 for each group comparison). There were no differences between the groups regarding the other angiographic findings. We observed that the previous use of medications, except oral anti-diabetic drugs, were similar between the groups.

In a full model, age (OR, 1.551; 95% CI, 1.118–2.025 when age changed from 55 to 66 years,

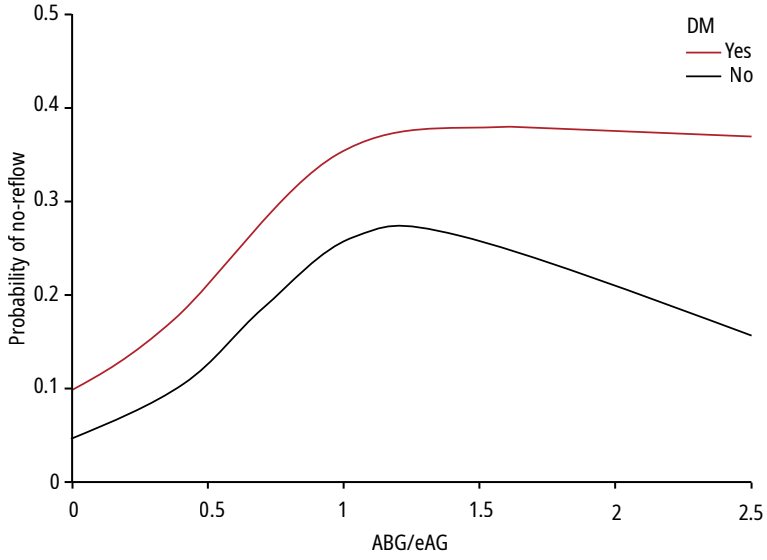

FIGURE 2 The interaction between the admission blood glucose to estimated average glucose ratio and no-reflow in patients with and without diabetes mellitus
Abbreviations: see TABLE 1 and FIGURE 1

diabetic (OR for ABG/eAG, 2.19; 95% CI, 1.16–4.16) and nondiabetic patients (OR for ABG/eAG, 2.37; 95% CI, 1.26–4.12) regarding the effect of ABG/eAG on NR (*P* for interaction = 0.826). In FIGURE 3, we show the relative importance of each predictor in the model. Among other parameters, the ABG/eAG ratio (contributing 25.3% of the explainable outcome in the model) was one of the strong predictors of NR in the present study. After the performance of a step-backward variable selection method, thrombus, the ABG/eAG ratio, the infarct-related artery diameter, and age remained in the reduced model. The differences in model fit, quality, and predictive accuracy were negligible and comparable (Supplementary material, *Table S1*).

We also drew a nomogram to predict the probability of NR using the reduced model (FIGURE 4). For example, when a 75-year-old STEMI patient without diabetes mellitus has the ABG/eAG ratio of 1, grade 3-thrombus, and an infarct-related diameter of 30 mm, the probability of NR is 30% during primary PCI.

P = 0.0012), the ABG/eAG ratio (OR, 2.274; 95% CI, 1.586–3.259 when ABG/eAG ratio changed from 0.91 to 1.23, *P* <0.001), the infarct-related artery diameter (OR, 0.843; 95% CI, 0.765–0.93 when the infarct-related artery diameter changed from 2.75 to 3 mm, *P* <0.001), and thrombus (OR, 1.869; 95% CI, 1.456–2.398 when thrombus changed from grade I to V, *P* <0.001) were associated with NR (TABLE 3 and FIGURE 1). FIGURE 2 shows that there was no significant interaction between the ABG/eAG and NR in patients with and without diabetes mellitus. Also, in a subgroup analysis, there were no significant subgroup differences between

DISCUSSION

The main finding of the current study is that a novel index, the ABG/eAG ratio, may be independently associated with NR both in diabetic and nondiabetic STEMI patients who were treated with primary PCI. To the best of our knowledge, this might be the first study showing a significant relationship between ABG/eAG ratio and NR in such patients.

Primary PCI is the recommended reperfusion strategy in all patients with STEMI, regardless of age.[15] However, the NR phenomenon may occur during the PCI, which overshadows the benefits

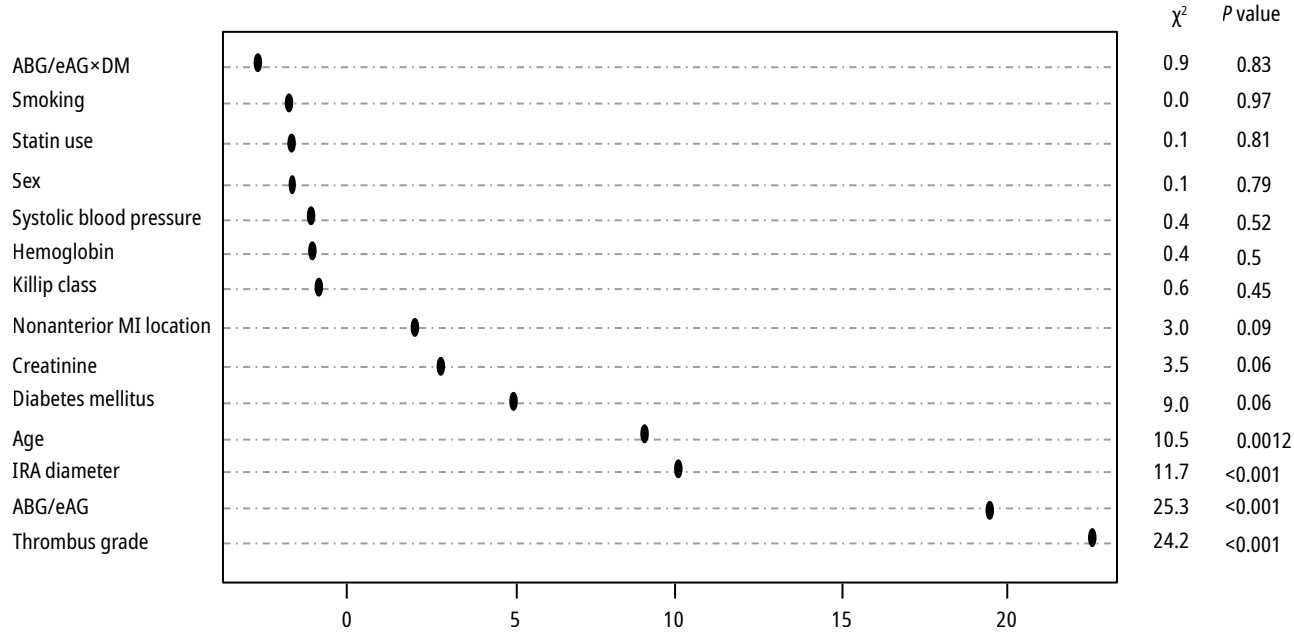

FIGURE 3 The relative significance of each predictor in the model
Abbreviations: see TABLES 1, 2, and 3

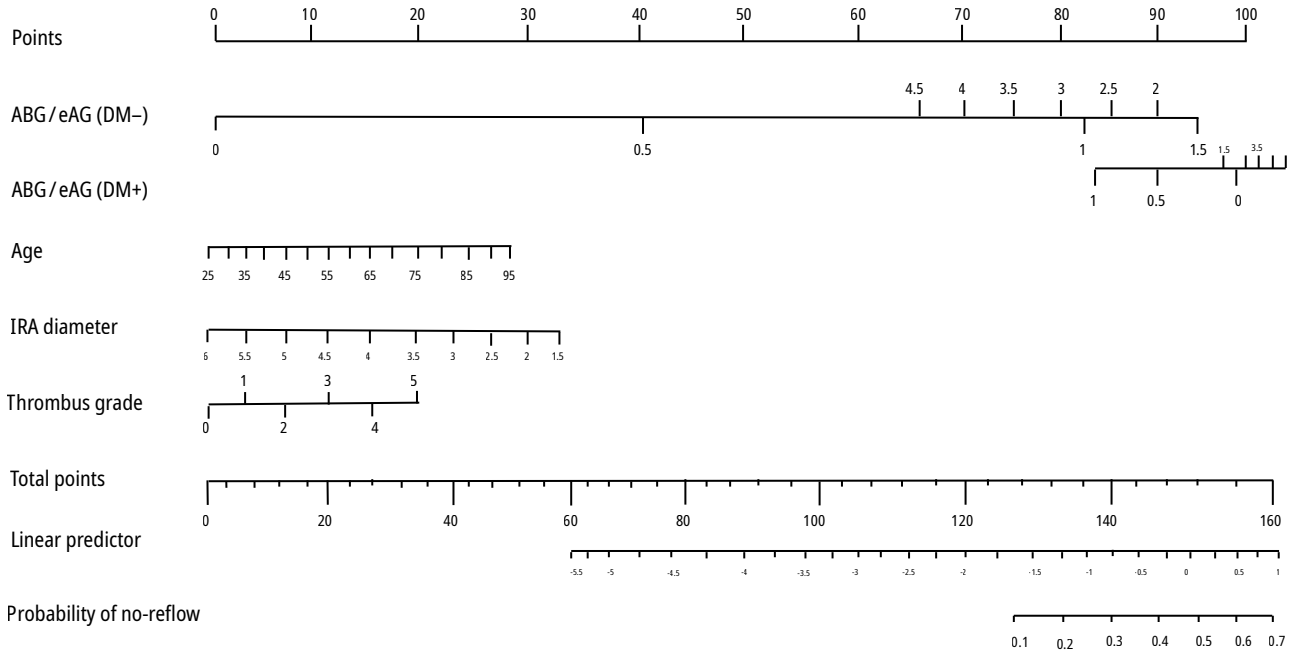

FIGURE 4 A nomogram showing the probability of no-reflow based on the admission blood glucose to estimated average glucose ratio, age, the infarct-related artery diameter, and the thrombus grade
Abbreviations: see TABLES 1 and 2, FIGURE 1

from this procedure. In particular, the incidence of NR is significantly higher in STEMI patients treated with primary PCI, and it may develop to a level as high as 20% to 30% according to previous studies.[16,17] In the present study, we observed that the incidence of NR was 22.7%, which was consistent with the aforementioned studies. Even though the exact underlying mechanism of NR has not been fully clarified, some clinical and angiographic parameters have been demonstrated to be independently related to the occurrence of NR.[18,19] Similarly, we found that age, thrombus grade, and the infarct-related diameter were significantly associated with NR in our model.

In patients admitted with acute coronary syndrome (ACS), acute hyperglycemia is a physiologic response to stress hormones, such as cortisol or epinephrine, due to the activation of the sympathetic system. Experimental studies have shown that an abrupt elevation of blood glucose during acute myocardial injury could lead to cellular and tissue injury by increasing the formation of free radicals in addition to inducing a prothrombotic state and endothelial dysfunction, thereby resulting in a larger infarct size.[20,21] Allying with these in vitro studies, observational clinical studies found that ABG level in STEMI was a powerful predictor of poorer survival rates and increased risk of major adverse cardiac events (MACEs), such as acute heart failure and NR, particularly in patients without preexisting diabetes.[22,23] However, because ABG only represents the stress response to acute myocardial injury and is related to increased stress hormones release, it may not be a true reflection of acute glucose levels, especially in diabetic STEMI patients.

HbA_{1c}, which can be used to estimate the eAG, reflects glucose levels over the past 2 or 3 months. It has been reported that chronic glucose elevation might have an adverse effect on both platelet and endothelial functions.[24] Besides that, it can cause apoptosis in cardiac myocytes.[25] However, in the literature, some published studies arrive at conflicting results as to whether this parameter is independently associated with increased risk of MACEs among patients with STEMI.[26,27]

The ABG/eAG ratio, which is a newly introduced index, combines both acute and chronic glucose levels.[9] Therefore, it may be accepted as indicating the true acute glycemic rise in critically ill patients, including STEMI patients. In a recent prospective study, which included 1553 consecutive ACS patients, Marenzi et al[10] found that the ABG/eAG ratio may be a better predictor of in-hospital MACEs and mortality than admission glycemia alone. Additionally, Gao et al[11] investigated this novel index for in-hospital morbidity and mortality only in STEMI patients undergoing primary PCI. On the basis of the study findings, they concluded that the ABG/eAG gives more significant in-hospital prognostic information than ABG alone, specifically in patients with diabetes and STEMI after primary PCI. However, the association of the ABG/eAG with NR in patients with STEMI treated with primary PCI was unknown until now. We demonstrated a stepwise increase of NR according to tertiles of the ABG/eAG. In addition, we provided evidence that there was no

interplay between the ABG/eAG ratio and NR in patients with and without preexisting diabetes. Moreover, we produced a practical nomogram in predicting the probability of NR for bedside use. Although the exact mechanism of NR with an elevated ABG/eAG ratio has not been clearly explained in the study, we considered the possibility that acute hyperglycemia and a chronic glycemic condition might impair microvascular function and cause platelet and endothelial dysfunction, thus leading to more frequent NR phenomena in patients with STEMI with and without diabetes. However, due to the design of the study, our findings require further prospective and large-scale studies to confirm the study results.

Limitations of the study Some limitations of our study should be noted before interpreting its results. The present study had a retrospective design; however, our cohort was relatively large, and consecutive patients were included in the study. Since patients with STEMI who were treated with primary PCI were included in the study, our results might not be generalizable to all ACS patients. We acknowledged that there might be a possible presence of residual confounding from unmeasured variables, which might affect the final outcome of the study. Additionally, NR was visually assessed only, and more specific and sensitive methods, including coronary flow reserve or cardiac magnetic resonance imaging, were not performed.

Conclusions The present study shows that there is a significant relationship between higher ABG/eAG ratio and NR in STEMI patients after primary PCI.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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