Research Article

EJCM E Journal of Cardiovascular Medicine

EJCM 2022;10(2):72-82

DOI: 10.32596/ejcm.galenos.2022.2021-12-072

Effect of Admission Hyperglycemia on Mortality in Diabetic and Non-diabetic Geriatric Patients with Non-ST-segment Elevation Myocardial Infarction

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Abstract

Objectives: High level of admission plasma glucose (APG) in myocardial infarction is associated with an increased risk of death in previous studies; however, most studies that evaluated this relationship were conducted before the guideline-based definition of hyperglycemia. This study was designed to assess the prognostic significance of APG and admission hyperglycemia in patients with and without diabetes mellitus (DM).

Materials and Methods: Five hundred and twenty-seven geriatric patients with non-ST segment elevation myocardial infarction (NSTEMI) were enrolled in the study. Patients were divided into four groups according to APG and DM status: those with DM, those with APG <144 mg/dL were named group 1, and those with APG ≥144 mg/dL were named group 2. Those without DM, those with APG <180 mg/dL were called group 3, and those with APG≥ 180 mg/dL were named group 4.

Results: Hyperglycemia was common in diabetic and nondiabetic patients threatening 29% of the study population. Patients without hyperglycemia (Groups 1 and 3) had the least mortality rates in one-month follow-up. In one-year follow-up, the patients with hyperglycemia (Group 2 and 4) had higher mortality rates (22.6% and 23.3%, respectively) than those with no-hyperglycemia groups. In regression analysis, hyperglycemia was independently associated with one-month and one-year mortality. In receiver operating characteristics curve analysis, the discriminative value of APG for one-month and one-year mortality was good in the groups.

Conclusion: APG may be used to predict one-month and one-year death irrespective of DM status. Therefore, DM and admission hyperglycemia could not be considered and treated as similar situations.

Keywords: Diabetes mellitus, acute myocardial infarction, non-ST-segment myocardial infarction, hyperglycemia, mortality

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Received: 12.12.2021 **Accepted:** 05.05.2022

Cite this article as: Demir Gündoğmuş P, Keskin Ü. Effect of Admission Hyperglycemia on Mortality in Diabetic and Non-diabetic Geriatric Patients with Non-ST-segment Elevation Myocardial Infarction. EJCM 2022;10(2):72-82.
DOI: 10.32596/ejcm.galenos.2022.2021-12-072

Introduction

Patients with Diabetes Mellitus (DM) have a higher risk of coronary artery disease and acute myocardial infarction (AMI) than the nondiabetic population. These patients more commonly encounter cardiovascular mortality[1]. Increased admission plasma glucose (APG) can be seen in the acute phase of AMI, ranging from 3% to 71% in patients without DM[2]. High plasma glucose levels might result from circulating stress hormones and pancreatic β-cell insufficiency that becomes apparent after a stressful event. Therefore, high APG levels might represent underlying metabolic derangement in most patients with AMI and be considered detrimental to jeopardized myocardium[3].

Several studies investigated the effect of APG on mortality and morbidity in patients with ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI). They demonstrated that high glucose levels increased the risk of mortality, stent thrombosis, recurrent AMI, and some studies showed inconsistent results on long-term mortality[1,4-6]. However, most of these studies were conducted before the percutaneous coronary intervention (PCI) era, and those patients were more commonly treated with thrombolytic therapy[1,3,4,7-10]. The primary treatment strategy in patients with AMI is PCI in the current era. There is a lack of evidence to establish the association between APG levels and outcomes in diabetic and nondiabetic patients with AMI undergone PCI.

In previous studies, various plasma glucose levels were defined as a cut-off value. However, according to a meta-analysis by Capes et al.[9] and American Diabetes Association (ADA) guideline, a plasma glucose level above 144 mg/dL in nondiabetic patients and a level above 180 mg/dL in diabetic patients were defined as hyperglycemia. These cut-off levels were not widely implemented in the previous studies[9,11-13].

The current study examined the utility of guideline-based hyperglycemia levels and the effect of APG levels on one-month and one-year mortality in patients with NSTEMI with and without DM. In the present study, the patients were categorized according to DM and hyperglycemia status, and the outcomes were compared between the groups and subgroups.

Materials and Methods

Study Population and Definitions

This retrospective study evaluated 568 consecutive geriatric patients with confirmed NSTEMI who were admitted to the emergency department of a tertiary hospital. The study duration was 18 months, from April 2017 to October 2018. NSTEMI was defined according to the European Society of Cardiology Guideline[14]. Patients were excluded with had followings: treated with thrombolytic therapy, no performed coronary angiography during the hospitalization, and no recorded glucose level in admission to the emergency department. Thirty-seven patients were excluded from the study based on the exclusion criteria, and four patients were not included in the study due to data loss after hospitalization. Therefore 527 patients with NSTEMI were enrolled in the study. A study flow chart was demonstrated in Figure 1. The primary endpoints were the one-month and one-year incidence of all-cause mortality.

Sociodemographic characteristics of the patients and necessary clinical information were obtained at the time of admission to the emergency department. Transthoracic echocardiography (TTE) evaluations of the patients were performed using the Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway). The patients' left ventricular ejection fraction (LVEF) was calculated by the Simpson method[15]. The study obtained local ethics committee approval, and the Helsinki Declaration principles were followed at all stages.

Diabetes Mellitus was defined as having a history of DM or following a DM-specific diet or using oral glucose-lowering medication and/or insulin, or HbA1c ≥6.5%. Hyperglycemia at admission was defined as blood glucose above 140 mg/dL upon patient admission to the hospital[11,12]. According to previous studies and a meta-

analysis by Capes et al.,[9] the prognostic cut-off is 144 mg/dL for patients without DM and 180 mg/dL for those with DM[3,9,16,17]. Patients were divided into four groups according to APG and DM status: those with DM, those with APG <144 mg/dL were named group 1, and those with APG ≥144 mg/dL were named group 2. Those without DM, those with APG <180 mg/dL were called group 3, and those with APG ≥180 mg/dL were named group 4.

Coronary Angiography, SYNTAX, Gensini and Grace Scores

The patients underwent coronary angiography (CAG) by either the femoral or radial approach using the standard Seldinger's technique. The synergy between percutaneous coronary intervention with Taxus and cardiac surgery (SYNTAX) score is a scoring system that emerged by scoring the lesions with 50% or more stenosis in vessels with a diameter of 1.5 mm and above in the images obtained by conventional CAG. Its relationship with mortality has been demonstrated (http://www.syntaxscore.com). Another scoring system used in the anatomical classification of coronary artery disease is Gensini scoring. Scoring is based on the extent of the lesion and the coronary artery in which it is located, and non-critical stenosis is also included in the scoring[18].

Global Registry of Acute Coronary Events (GRACE) scoring is a mortality predictive scoring system that uses clinical parameters such as age, heart rate, systolic blood

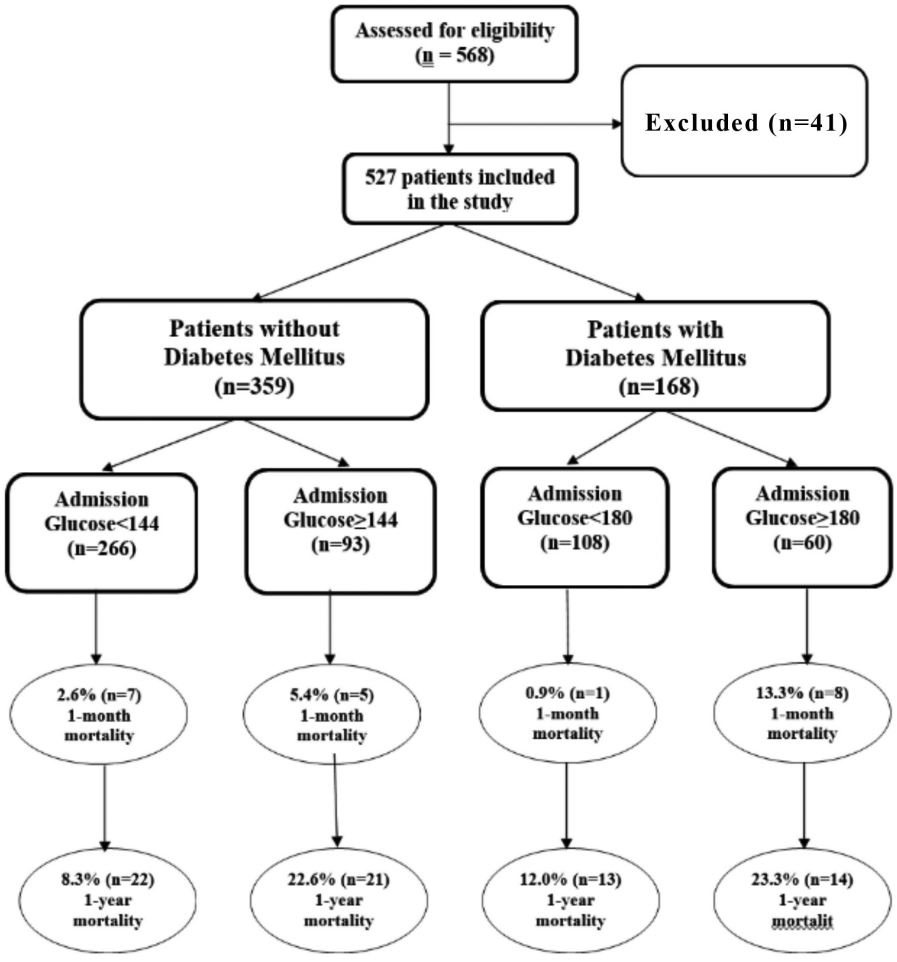

Figure 1. Flow chart of the study

pressure, baseline creatine level, history of congestive heart failure, in-hospital percutaneous coronary intervention, history of AMI, cardiac enzyme levels, ST-segment depression on admission electrocardiography (ECG)[19]. This study used single serum levels of cardiac troponin I (cTnI) 0.1 ng/mL as the elevated cardiac enzyme. ST-segment depression was defined as decreased ST segment 0.5 mV below the isoelectric line in any ECG lead.

Statistical Analysis

Analyses of the study were performed using SPSS version 22.0 (IBM SPSS, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables as numbers and percentages. After evaluating the parametric assumptions, the intergroup comparison of continuous variables was compared using a one-way analysis of variance. The statistical difference between the groups was assessed with the Tukey post-hoc test. Pearson's chi-square was used to compare categorical variables. Survival analyzes of the four groups were evaluated using the Kaplan-Meier survival method. The log-rank test was used to analyze the differences between groups. Multivariate analyzes were evaluated with the Cox proportional regression model. The hazard ratio (HR) was used for the groups' relative risk of death. In multivariate models, confounders in multivariate analysis were considered predictors of 1-month and 1-year mortality. P value <0.05 was considered statistically significant.

Results

Patients' baseline characteristics are listed in Table 1. The groups were similar in terms of age, current smoking, prior stroke, and anticoagulant therapy. There was a higher rate of female subjects, chronic kidney disease, hypertension, atrial fibrillation, previous peripheral arterial disease, coronary artery disease, renin-angiotensin system blockers, and P2Y12 inhibitors used in the DM group (Groups 3 and 4) compared to the non-DM group (Groups 1 and 2). Patients with DM and hyperglycemia (Group 4) had a significantly higher rate of chronic lung disease, hypertension, and using aspirin than the other three groups. The number of patients using calcium channel blockers was higher in both DM and non-DM groups without hyperglycemia (Groups 1 and 3).

Patients' clinical characteristics, treatment strategy, discharge medication, and outcomes were summarized in Table 2. The groups were similar in terms of ST-segment deviation, revascularization, admission heart rate, GRACE score, and hospitalization duration. The patients with DM and hyperglycemia (Group 4) had higher admission systolic blood pressure, SYNTAX I, SYNTAX II and Gensini scores, HbA1C and APG levels compared to the other groups. Additionally, Group 4 had lower LVEF, hemoglobin and estimated glomerular filtration rate (eGFR) levels compared to other groups. Whereas the patients with hyperglycemia (Group 2 and 4) were more commonly treated with conservative strategy, the patients with non-DM and hyperglycemia (Group 1) more commonly underwent PCI, and were less commonly treated with conservative strategy and coronary artery bypass grafting (CABG). According to discharge medication, P2Y12 inhibitor use was more common in groups 1 and 3 due to the revascularization strategy. Anticoagulant therapy was more commonly used in DM because the existence of DM would increase the CHA2DS2-VASc score. Statins were less commonly used in patients with DM and hyperglycemia (Group 4), probably due to side effects.

Group 4 had a higher mortality rate (13.3%) in one-month follow-up, whereas Group 3 had a lower mortality rate (0.9%) compared to the other two groups. Patients without hyperglycemia at admission (Groups 1 and 3) had the least mortality rate. In one-year follow-up, the patients with hyperglycemia (Groups 2 and 4) had higher mortality rates (22.6% and 23.3%, respectively) compared to the patients who had no hyperglycemia. Overall survivals for Groups 1, 2, 3 and 4 were 89.0%, 72.0%, 87.0% and 63.3% respectively. Therefore, during the one-year follow-up, Group 4 had lower overall survival than the other three groups, and Group 2 had lower overall survival compared to Groups 1 and 2. Kaplan-Meier overall cumulative risk

of groups regarding mortality was demonstrated in Figure 2, and the log-rank test p value was <0.001. According to receiver operating characteristics (ROC) curve analysis, the admission glucose level of 157 mg/dL was identified as an effective cut-off point for one-month mortality [area under the curve (AUC): 0.86; 95% confidence interval (CI): 0.68-0.85, p<0.001], and it had a sensitivity of 76% and specificity of 71%. The discriminative value of admission glucose for one-month mortality was also good in DM and non-DM groups (AUC was 0.74 for patients with DM and 0.76 for patients with non-DM) (Figure 3). Additionally, the admission glucose level of 138 mg/dL was identified as an effective cut-off point for one-year mortality (AUC: 0.67; 95% CI: 0.60-0.74, p<0.001), and it had a sensitivity of 72% and specificity of 62%. The discriminative value of APG for one-month mortality was also good in DM and non-DM groups (AUC was 0.60 for patients with DM and 0.67 for patients with non-DM) (Figure 4).

Table 3 presents the study population's one-month and one-year univariate and multivariable Cox regression analyses. Univariate predictors of one-month mortality were GFR <60 mL/min/1.73 m^2, LVEF <50% and hyperglycemia. By multivariate regression analysis, the two independent factors that increased the risk of one-month mortality were GFR <60 mL/min/1.73 m^2 (HR:

Table 1. Baseline characteristics of groups according to diabetes mellitus and hyperglycemia status

Variables	No diabetes mellitus		Diabetes mellitus		p value
	Group 1 Glucose <144 mg/dL (n=266)	Group 2 Glucose ≥144 mg/dL (n=93)	Group 3 Glucose <180 mg/dL (n=108)	Group 4 Glucose ≥180 mg/dL (n=60)	
Age, year	76.44±6.60	76.37±7.06	75.45±6.10	77.01±6.92	0.458
Female gender	100 (37.6%)$^{£β}$	43 (46.2%)$^{£β}$	71 (65.7%)$^{*#}$	40 (66.7%)$^{*#}$	<0.001
Current smoking	44 (16.5%)	7 (7.5%)	13 (12.0%)	5 (8.3%)	0.085
Chronic lung disease	22 (8.3%)^{β}	13 (14.0%)^{β}	10 (9.3%)β	17 (28.3%)$^{*#£}$	<0.001
Chronic kidney disease	165 (62.0%)$^{£}$	58 (62.4%)$^{£}$	92 (85.2%)$^{*#β}$	41 (68.3%)$^{£}$	<0.001
Hypertension	174 (65.4%)$^{£β}$	60 (64.5%)$^{£β}$	90 (83.3%)$^{*#}$	53 (88.3%)$^{*#}$	<0.001
Atrial fibrillation	40 (15.0%)$^{£β}$	18 (19.4%)$^{£}$	37 (37.3%)$^{*#}$	16 (26.7%)*	<0.001
Prior PAD	14 (5.3%)$^{£β}$	4 (4.3%)$^{£β}$	0 (0%)$^{*#β}$	8 (13.3%)$^{*#£}$	0.002
Prior CAD	121 (45.5%)$^{#}$	20 (21.5%)$^{*£β}$	50 (46.3%)$^{#}$	35 (58.3%)$^{#}$	<0.001
Prior PCI	56 (21.1%)$^{#}$	8 (8.6%)$^{*£}$	30 (27.8%)$^{#}$	10 (16.7%)	0.006
Prior stroke	13 (4.9%)	0 (0%)	5 (4.6%)	4 (6.7%)	0.146
Admission medications					
Aspirin	128 (48.1%)	34 (36.6%)^{β}	46 (42.6%)^{β}	37 (61.7%)$^{#£}$	0.017
P2Y12 inhibitors	66 (24.8%)$^{#β}$	9 (9.7%)$^{*£β}$	28 (25.9%)$^{#}$	23 (38.3%)$^{*#}$	<0.001
Warfarin	21 (7.9%)	16 (17.2%)	9 (8.3%)	8 (13.3%)	0.056
NOAC	20 (7.5%)	4 (4.3%)	8 (7.4%)	4 (6.7%)	0.755
RAS blockers	127 (47.7%)$^{£β}$	37 (39.8%)$^{£β}$	69 (63.5%)$^{*#}$	38 (63.3%)$^{*#}$	<0.001
Beta blockers	149 (56.0%)	38 (40.9%)	61 (56.5%)	32 (53.3%)	0.072
CCB	95 (35.7%)^{β}	24 (25.8%)$^{£β}$	44 (40.7%)$^{#}$	11 (18.3%)$^{*£}$	0.008

The p value indicates the statistical difference between the 4 groups.
*p<0.05, vs. group 1
$^{#}$p<0.05, vs. group 2
$^{£}$p<0.05, vs. group 3
^{β}p<0.05, vs. group 4
CAD: Coronary artery disease, CCB: Calcium channel blockers, NOAC: Novel anticoagulation drugs, PAD: Peripheral arterial disease, PCI: Percutaneous coronary intervention, RAS: Renin-angiotensin system, n: Number

Table 2. Clinical characteristics of groups according to Diabetes Mellitus and hyperglycemia status

Variables	No diabetes mellitus		Diabetes mellitus		p value
	Group 1 Glucose <144 mg/dL (n=266)	Group 2 Glucose ≥144 mg/dL (n=93)	Group 3 Glucose <180 mg/dL (n=108)	Group 4 Glucose ≥180 mg/dL (n=60)	
ST segment deviation	74 (27.8%)	26 (28.0%)	39 (36.1%)	23 (38.3%)	0.213
Revascularization	188 (70.7%)	56 (60.2%)	74 (68.5%)	38 (63.3%)	0.261
Hear rate (beat/min)	82.29±20.14	84.78±15.85	83.25±18.74	87.56±19.17	0.427
Systolic blood pressure (mmHg)	132.22±22.66$^{\beta}$	131.29±20.23$^{\beta}$	129.87±14.32$^{\beta}$	139.56±19.19$^{*\#£}$	0.026
Diastolic blood pressure (mmHg)	77.71±12.04	76.34±10.40	75.00±13.96	79.30±9.38	0.097
LVEF (%)	51.86±9.65$^{\beta}$	49.24±9.46	50.87±8.65$^{\beta}$	45.88±9.02$^{*£}$	<0.001
SYNTAX Score	10.66±9.22$^{\beta}$	10.62±9.98$^{\beta}$	10.26±9.17$^{\beta}$	16.72±13.43$^{*\#£}$	0.001
SYNTAX II-1 Score	37.63±9.08$^{\beta}$	40.04±9.84$^{\beta}$	40.29±8.81$^{\beta}$	47.30±13.90$^{*\#£}$	<0.001
SYNTAX II-2 Score	36.56±9.19$^{£\beta}$	36.78±8.47$^{£\beta}$	32.83±6.35$^{*\#\beta}$	41.93±10.53$^{*\#£}$	<0.001
Grace Score	136.83±21.25	141.78±29.52	134.43±18.18	142.00±24.20	0.088
Gensini Score	29.02±20.18$^{\beta}$	25.11±22.60$^{\beta}$	30.45±20.68$^{\beta}$	41.59±31.24$^{*\#£}$	0.002
HbA1C	5.98±0.93$^{\beta}$	5.90±0.41$^{\beta}$	5.95±0.67$^{\beta}$	8.18±2.62$^{*\#£}$	<0.001
Glucose	105.05±18.05$^{\#£\beta}$	189.56±58.66$^{*£\beta}$	125.37±32.73$^{*\#\beta}$	244.36±43.58$^{*\#£}$	<0.001
Hemoglobin (mg/dL)	13.11±1.95$^{£\beta}$	13.12±1.74$^{£\beta}$	12.06±1.96$^{*\#}$	11.96±1.78$^{*\#}$	<0.001
eGFR (mL/min/1.73 m^2)	56.71±18.37$^{\beta}$	53.45±19.36	51.82±15.86	48.27±21.52*	0.005
Treatment strategy					
Conservative	78 (29.3%)	37 (39.8%)	34 (31.5%)	22 (36.7%)	0.020
PCI	171 (64.3%)	43 (46.2%)	58 (53.7%)	31 (51.7%)	
CABG	17 (6.4%)	13 (14.0%)	16 (14.8%)	7 (11.6%)	
Hospitalization days	6.44±6.77	7.75±6.95	6.01±4.25	6.68±4.97	0.227
Discharge medications					
Aspirin	235 (88.3%)$^{\#}$	69 (74.2%)*	90 (83.3%)	48 (80.0%)	0.011
P2Y12 inhibitors	222 (83.5%)$^{\#}$	61 (65.6%)$^{*£}$	90 (83.3%)$^{\#}$	46 (76.7%)	0.002
Warfarin	21 (7.9%)$^{\#\beta}$	16 (17.2%)*	13 (12.0%)	10 (16.7%)*	0.045
NOAC	16 (6.0%)$^{£\beta}$	8 (8.6%)$^{£}$	24 (22.2%)$^{*\#}$	8 (13.3%)*	<0.001
RAS blockers	117 (66.5%)	55 (59.1%)$^{£\beta}$	80 (74.1%)$^{\#}$	47 (78.3%)$^{\#}$	0.038
Beta-Blockers	241 (90.6%)	79 (84.9%)	97 (89.8%)	50 (83.3%)	0.251
Statins	190 (71.4%)$^{\beta}$	64 (68.8%)$^{\beta}$	76 (70.4%)$^{\beta}$	22 (36.7%)$^{*\#£}$	<0.001
Follow-up time (months)	11.8±2.2$^{\beta}$	10.7±3.4	11.3 ± 2.5$^{\beta}$	10.9 ± 4.4$^{*£}$	<0.001
One-month mortality	7 (2.6%)$^{\beta}$	5 (5.4%)$^{£}$	1 (0.9%)$^{\#\beta}$	8 (13.3%)$^{*£}$	<0.001
One-year mortality	22 (8.3%)$^{\#\beta}$	21 (22.6%)$^{*£}$	13 (12.0%)$^{\#\beta}$	14 (23.3%)$^{*£}$	<0.001

Abbreviations: CABG: Coronary artery bypass grafting, eGFR: Estimated glomerular filtration rate, LVEF: Left ventricular ejection fraction, NOAC: Novel anticoagulation drugs, PCI: Percutaneous coronary intervention, RAS: Renin-angiotensin system.
p value indicates the statistical difference between the 4 groups.
$^{*}P < 0.05$, vs. Group 1
$^{\#}P < 0.05$, vs. Group 2
$^{£}P < 0.05$, vs. Group 3
$^{\beta}P < 0.05$, vs. Group 4

9.66, 95% CI: 1.28-72.4) and hyperglycemia (HR: 4.16, 95% CI: 1.71-10.09). Univariate predictors of one-year mortality were female gender, the age between 65-74 years, ST-segment deviation, eGFR <60 mL/min/1.73 m^2, LVEF <50%, hyperglycemia and SYNTAX score. By multivariate regression analysis, the four independent factors that increased the risk of one-year mortality were the age between 65-74 years (HR: 5.77, 95% CI: 2.49-13.35), ST-segment deviation (HR: 2.65, 95% CI: 1.51- 4.65), LVEF<50% (HR: 5.77, 95% CI: 2.49-13.35) and hyperglycemia (HR: 1.87, 95% CI: 1.10-3.19). DM was associated neither with one-month nor one-year mortality.

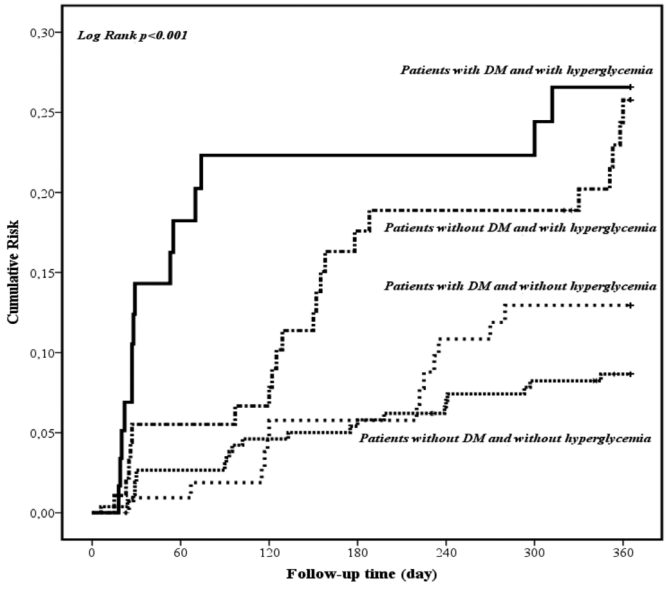

Figure 2. Kaplan-Meier overall cumulative risk of groups regarding mortality

DM: Diabetes mellitus

Discussion

Two significant results were obtained in this study, in which we evaluated the short-term and long-term effects of APG levels in NSTEMI patients. First, hyperglycemia was common in diabetic and nondiabetic patients, threatening approximately 29% of all NSTEMI patients. Second, hyperglycemia was independently associated with short and long-term overall death in both diabetic and nondiabetic patients. The present study demonstrated that patients who were not diagnosed with DM at the time of AMI admission but whose APG levels were in the diabetic range had a similar mortality trend in patients with a previous diagnosis of diabetes. Additionally, the diabetic-hyperglycemic group (Group 4) was more commonly associated with some

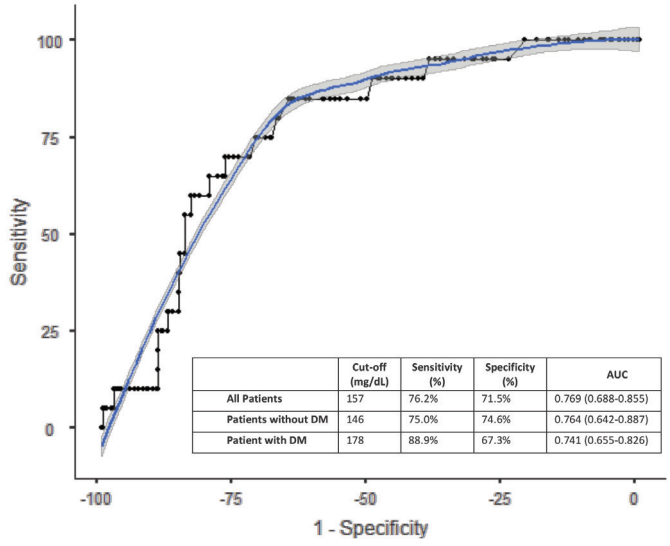

Figure 3. ROC curve of APG one-month mortality

ROC: Receiver operating characteristics, APG: Admission plasma glucose, AUC: Area under the curve, DM: Diabetes mellitus

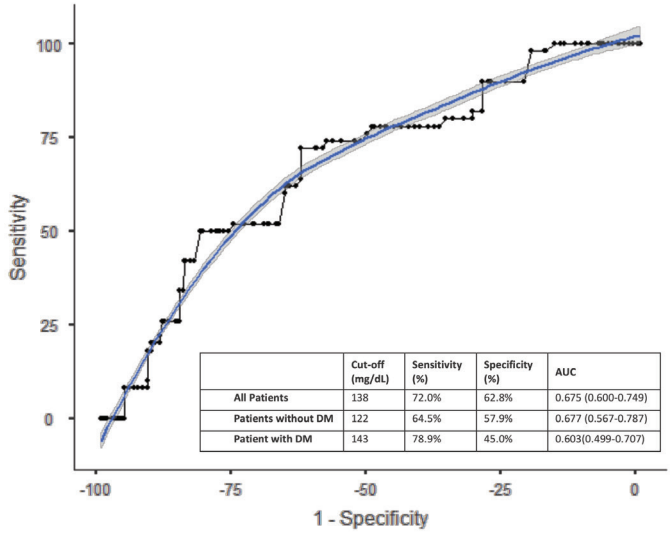

Figure 4. ROC curve of APG mortality from one month to one year

ROC: Receiver operating characteristics, APG: Admission plasma glucose, AUC: Area under the curve, DM: Diabetes mellitus

unfavorable clinical and angiographic characteristics such as lower LVEF, lower eGFR and higher SYNTAX and Gensini scores.

This study not only confirms the association between APG level and mortality after NSTEMI, but also expresses the importance of this variable as a predictor of long-term mortality in diabetic and nondiabetic patients. We showed that patients without a diagnosis of DM but with APG levels in the diabetic range have a similarly high risk of death as patients with DM.

There are some possible underlying mechanisms of the high APG levels in patients with AMI, such as growth hormone and activation of stress hormones (noradrenaline, glucagon, cortisol)[7,9,20]. During ischemia, glucose level increases as a compensatory mechanism to protect myocardial contraction and prevent myocyte necrosis[21]. The other possible mechanism in STEMI patients is that high glucose levels facilitate platelet adhesion and aggregation by accelerating inflammatory processes and directly activating the glycation of coagulation factors[22-24]. Thus, a vicious cycle occurs between myocardial ischemia and glucose.

According to literature and previous studies, some authors demonstrated an association between microvascular coronary obstruction and high APG levels[16,17,25-27]. Straumann et al.[25] examined the predictive value of APG in patients who underwent primary PCI, and they classified the patients according to plasma glucose levels at admission: <7.8 mmol/L, 7.8 to 11 mmol, and >11.0 mmol/L. However, their categorization strategy was not based on a guideline, and they did not stratify the patients according to their diabetes diagnosis[25]. Kosiborod et al.[16] evaluated a national sample of elderly patients with AMI, and in

Table 3. Predictors of One-month and One-year mortality: Cox regression analysis

Predictors	Univariable		Multivariable	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
One-Month Mortality				
Gender (female)	0.453 (0.183-1.123)	0.087		
Age (65-74 years)	0.974 (0.410-2.311)	0.952		
ST-segment deviation	2.075 (0.881-4.887)	0.095		
Diabetes mellitus	1.633 (0.688-3.875)	0.266		
eGFR<60 (mL/min/1.73 m²)	9.886 (1.327-73.660)	0.025	9.662 (1.288-72.492)	0.027
LVEF <50%	3.022 (1.172-7.789)	0.022	2.232 (0.858-5.803)	0.100
Hyperglycemia	4.130 (1.712-9.966)	0.002	4.164 (1.717-10.099)	0.002
SYNTAX score	1.034 (0.989-1.082)	0.142		
One-year mortality				
Gender (female)	0.372 (0.223-0.620)	<0.001	0.850 (0.479-1.508)	0.578
Age (65-74 years)	2.849 (1.609-5.043)	<0.001	5.776 (2.499-13.350)	<0.001
ST-segment deviation	2.146 (1.342-3.431)	<0.001	2.654 (1.515-4.650)	0.001
Diabetes mellitus	1.382 (0.854-2.236)	0.188		
eGFR<60 (mL/min/1.73 m²)	2.524 (1.356-4.700)	0.004	0.884 (0.451-1.732)	0.719
LVEF <50%	3.875 (2.324-6.461)	<0.001	2.654 (1.515-4.650)	0.001
Hyperglycemia	2.680 (1.677-4.282)	<0.001	1.876 (1.102-3.193)	0.020
SYNTAX score	1.032 (1.008-1.057)	0.008	1.020 (0.998-1.042)	0.065

eGFR: Estimated glomerular filtration rate, LVEF: Left ventricular ejection fraction, SYNTAX: Synergy between percutaneous coronary intervention with taxus and cardiac surgery, CI: Confidence interval

their analysis, APG was categorized into ≤110, >110 to 140, >140 to 170, >170 to 240, and >240 mg/dL) for its association with mortality in patients with and without recognized DM. Although they did not determine a single cut-off value for hyperglycemia, their patient population was not homogenous. Additionally, they classified the patients as having recognized DM if their medical records contained documentation of a previous history of DM. However, they could not use HbA1C levels to differentiate the patients better. Zhao et al.[28] reported a meta-analysis in 2015 which included 13 studies and demonstrated a significant relationship between the APG levels and long-term mortality. However, they did not find any relationship with short-term mortality[28]. Furthermore, they only included studies that enrolled the patients with STEMI. There is no convincing data on this subject.

The utilization of HbA1C levels in routine clinical practice made an enormous contribution to the rapid detection of DM. The patients without any medication on DM or documented DM might be in a group of old onset DM with no hospital records. The lack of utilization of HbA1C levels in most previous studies might have caused an underestimation of the rate of the diabetic patient population[3-6,16,17,25,26,29]. We checked HbA1C levels in all patients to diagnose DM accurately, which was not done in most previous studies.

Additionally, most studies evaluating the effect of APG levels on clinical outcomes in patients with AMI were reported before the investigations to determine a single cut-off value by meta-analyses, large-scale studies, clinical guidelines, and the statement of the definition "hyperglycemia" by ADA[2,30-33]. In the current study, hyperglycemia was defined as admission APG measurement >140 mg/dL in nondiabetic patients in accordance with the 2013 ADA Standard of Medical Care Criteria which are based on some studies with large patient populations.

Study Limitations

Our study has several limitations. First, due to a relatively low number of patients in subgroups, we did not further check the discriminative value of APG levels in different treatment strategies. Second, we could not reach the socioeconomic status, immunological and infectious status, obesity, and physical activity data and could not adjust the analysis for these confounders. Third, we did not evaluate the patients' further glucose measurements during the hospitalization and the therapeutic interventions for hyperglycemia.

Conclusion

Our study evaluated the effect of APG and the newly generated term of "hyperglycemia" in overall patients with NSTEMI, and confirmed that APG might be an important prognostic indicator of short and long-term mortality, and novel hyperglycemia cut-off values might be used as a simple prognostic threshold in these patients. As far as we know, the present study is the first to evaluate recommended cut-off APG separately in patients with NSTEMI regardless of the treatment strategy. Furthermore, we investigated the association of APG with several widely used angiographic and clinical scores. Our results warrant further investigations with large-scale studies.

Ethics

Ethics Committee Approval: Haydarpaşa Numune Training and Research Hospital Ethics Committee approval (no: 2017/117, date: 05.09.2018) was obtained for the study.

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and/or Medical Practices: Demir-Gündoğmuş P, Keskin Ü, Concept: Demir-Gündoğmuş P, Design: Demir-Gündoğmuş P, Keskin Ü, Data Collection and/or Processing: Demir-Gündoğmuş P, Keskin Ü, Analysis

and/or Interpretation: Demir-Gündoğmuş P, Literature Search: Demir-Gündoğmuş P, Keskin Ü, Writing: Demir-Gündoğmuş P, Keskin Ü.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: No financial support was received from any source for this study.

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