European Journal of Therapeutics

DOI: 10.5152/EurJTher.2019.18055

Original Research

The Relationship between Admission HbA1c Level and Infarct–Related Artery Patency in ST Elevation Myocardial Infarction Patients

Muhammet Cihat Çelik[1], Abdullah Nabi Aslan[2], Ahmet Korkmaz[1], Murat Can Güney[3], Yunus Emre Özbebek[3], Ümit Güray[1]

[1]Clinic of Cardiology, Ankara Numune Training and Research Hospital, Ankara, Turkey

[2]Clinic of Cardiology, Atatürk Training and Research Hospital, Ankara, Turkey

[3]Department of Cardiology, Ankara Yıldırım Beyazıt University School of Medicine, Ankara, Turkey

ABSTRACT

Objective: Patency of infarct-related artery (IRA) in patients with ST segment elevation myocardial infarction (STEMI) before primary percutaneous coronary intervention (pPCI) is associated with lower mortality and better clinical outcome. This study aimed to investigate the relationship between admission hemoglobin A1c (HbA1c) and IRA patency before mechanical reperfusion in patients with STEMI.

Methods: A total of 140 consecutive patients with STEMI undergoing pPCI within 12 h from symptom onset were retrospectively evaluated. The IRA patency was assessed by the thrombolysis in myocardial infarction (TIMI) flow grade. Patients were initially divided into two groups based on the TIMI flow grade. Impaired flow was defined as TIMI grades 0 and 1, and normal flow or patency was defined as TIMI 2 and 3. Patients were divided into three groups based on admission HbA1c levels as group I (HbA1c ≤ 5.6%), group II (HbA1c 5.6%–6.5%), and group III (HbA1c ≥ 6.5%).

Results: Among 140 patients, 46 (32.8%) had pre-pPCI TIMI 2 and 3 flow in IRA. The IRA patency was found to be similar in all three HbA1c groups (p=0.269). Admission HbA1c levels were similar in both IRA groups (p=0.314). In multivariate regression analysis, only MPV (OR:0.589, 95%CI:0.365–0.951, p=0.030) was significantly and independently associated with IRA patency.

Conclusion: HbA1c is not an independent predictor of the IRA patency in patients with STEMI treated with pPCI. However, MPV is a simple, low-cost, and easily accessible parameter and might be used as a predictor of IRA patency.

Keywords: HbA1c, infarct-related artery patency, mean platelet volume, primary percutaneous coronary intervention, ST elevation myocardial infarction

INTRODUCTION

Coronary heart disease (CHD) and its subgroup acute myocardial infarction (AMI) are the leading causes of mortality in our country and world wide (1, 2). AMI, also known as ST segment elevation myocardial infarction (STEMI), has high mortality rates with poor prognosis after survival (3). In STEMI, primary percutaneous coronary intervention (pPCI) is accepted as the reference therapeutic strategy (4).

Diabetes mellitus (DM) is a systemic metabolic disease associated with hyperglycemia, dyslipidemia, glycosuria, and accompanying clinical symptoms and biochemical findings. DM is regarded as a CHD risk equivalent. CHD is the most common cardiovascular (CV) complication that leads to morbidity and mortality in patients with DM (5). A patient with diabetes has 2-4 fold increased risk of CV mortality as compared to patients not suffering from diabetes. In this patient group, the CV diseases are responsible for 70%-80% of mortality. In patients with diabetes, blood glucose levels and exposure time to hyperglycemia are major risk factors for development of microvascular complications (6). However, there is no evidence that proves the same relation between blood glucose levels and exposure time to hyperglycemia and macrovascular complications (7, 8).

Hemoglobin A1c (HbA1c) is routinely used as a marker of long-term glycemic control and is unaffected by acute perturbations. The HbA1c levels could give us a better insight to understand the relation between long-term glycemic control and complications of hyperglycemia. On the other hand, studies investigating the relation between HbA1c and mortality have failed to demon-

How to cite: Çelik MC, Aslan AN, Korkmaz A, Güney MC, Özbebek YE, Güray Ü. The Relationship between Admission HbA1c Level and Infarct–Related Artery Patency in ST Elevation Myocardial Infarction Patients. Eur J Ther 2019; 25(4): 304–11.

ORCID IDs of the authors: M.C.Ç. 0000–0002–6496–7849; A.N.A. 0000–0001–9392–3311; A.K. 0000–0003–2672–5109; M.C.G. 0000–0001–5364–1360; Y.E.Ö. 0000–0002–4556–9693; Ü.G. 0000–0002–6604–2970

Corresponding Author: Abdullah Nabi Aslan **E–mail:** drnabiaslan@hotmail.com

Received: 30.10.2018 • **Accepted:** 21.08.2019

strate a direct relation (9, 10). Many studies have proved that in patients with diabetes, DM with poor glycemic control is related with CHD severity (11). But these previous studies generally focused on long-term mortality and CV events instead of acute incidences.

Infarct-related artery (IRA) is defined as the stenotic coronary artery with atheroma or thrombus that is responsible for acute coronary syndrome (ACS) (12). Early IRA patency is associated with better clinical outcomes in patients with STEMI (13-16). Huge data are present in the literature regarding factors affecting IRA patency .Previous studies have proved that some proinflammatory and prothrombotic biomarkers such as NLR (neutrophil to lymphocyte ratio), PLR (platelet to lymphocyte ratio), and RDW (red blood cell distribution width) are related with pre-pPCI IRA patency (17-19). However, no study in the literature investigates the direct relationship between HbA1c levels and pre-PCI IRA patency. Therefore, the relation between admission HbA1c levels and pre-PCI IRA patency in patients with STEMI was investigated in this study.

METHODS

Subjects

This is a retrospective study performed on patients admitted to our hospital with the diagnosis of STEMI between January 2016 and December 2016. A total of 140 patients without previously known CHD and chronic kidney disease who were diagnosed with STEMI in the first 12 hof chest pain and received pPCI were included in this study. The patients were divided into three groups according to baseline HbA1c levels in accordance with ADA criteria (20). As a result, 35 patients with HbA1c levels <5.6%, 65 patients with HbA1c levels between 5.6% and 6.5%, and 40 patients with HbA1c levels >6.5%were investigated. Seven patients in the HbA1c >6.5% group did not have DM diagnosis and diagnosed as new DM according to our findings. Patients deceased during the pPCI procedure, those who presented after 12 h of chest pain, and those who refused the pPCI procedure were excluded from the study.

Ankara Numune Training and Research Hospital ethics committee approved the study (date: 22.02.2017, no: E-17-1248), and all subjects provided informed consent to participate in the study. All patients were treated in accordance with European Society of Cardiology guidelines (21).

Angiographic Evaluation

Selective left and right coronary angiography (CAG) was performed in all cases using the Judkins technique with Siemens Axiom Artis Zee and Shimadzu IVR master systems. Experienced (>75 cases/year) interventional cardiologists performed the CAG and pPCI procedures. Coronary arteries were visualized in right and left oblique positions with cranial, caudal, and antero-posterior views. Angiographic images were evaluated with calibration techniques for the degree of stenosis. Critical coronary artery stenosis was accepted as >50% stenosis for left main coronary artery and >70% for other epicardial arteries. The IRA patency was defined as TIMI 2-3 flow in the distal vascular segment, while TIMI 0-1 flow was evaluated as non-patent artery (22).

Biochemical Evaluation

Hemoglobin A1c levels were evaluated by immunoturbidimetric method with Cobas 6000 device.

Statistical Analysis

All data were analyzed by using Statistical Package for the Social Sciences 20.0 statistical software package (SPSS IBM Corp.; Armonk, NY, USA). The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. The normally distributed variables were presented as average ± standard deviation. For all other numerical variables, the reported values were corresponded to the medians. The categorical variables were given with their frequencies and the associated percentages. When analyzing the differences among the parametric variables, the one-way analysis of variance test was used for multiple-group comparisons, and the post-hoc Scheffe test was used for group-by-group comparisons. For non-parametric variables, Kruskal-Wallis test was used for multiple-group comparisons, and the Mann-Whitney U test was used for group-by-group comparisons. Categorical variables were compared with χ^2 and Fisher's exact tests. The predictors for IRA dilation patency were determined using multivariate logistic regression with backward elimination. All base-demographic features, CV characteristics, and laboratory parameters that led to p-values smaller than 0.10 in univariate analyses were included in the multivariate analyses. A p value <0.05 was considered statistically significant.

RESULTS

Patients' Characteristics

Patient groups according to baseline characteristic features are summarized in Table 1. A total of 140 patients were divided into three groups as group 1 (HbA1c ≤5.6%, n=35), group 2 (HbA1c 5.6%-6.5%, n=65), and group 3 (HbA1c ≥6.5%, n=40). According to post-hoc analyses, patients in group 3 were significantly older than those in group 1 (p=0.002). The number of male patients in group 3 was significantly lower compared to the other groups (p=0.003). There were more patients with hypertension in groups 2 and 3 compared to those in group 1 (group 1-2, p=0.046; group 1-3, p=0.001). On the other hand, there was no statistical significance for hypertension prevalence between groups 2 and 3 (p=0.103). As expected, DM prevalence was higher in group 3 (p<0.001), whereas it was similar between groups 1 and 2 (p=0.155). Among 40 patients in group 3, 33 patients have already had DM diagnosis and 7 patients got new diagnosis according to the current guidelines. Smoking rates were significantly lower in group 3 than groups 1 and 2 (p=0.035). There were no statistically significant differences between the three groups in terms of hyperlipidemia incidence, family history for CHD, left ventricular ejection fraction, and chest pain to CAG time.

Laboratory Findings

The laboratory findings of study population are listed in Table 2. According to these findings, blood glucose levels at the time of admission were significantly higher in patients with HbA1c levels >6.5% (p<0.001). On the other hand, there was no significant difference in blood glucose levels between groups 1 and 2. In addition, hemoglobin levels were significantly higher inpatients in group 1 than those in group 3 (p=0.033). However, neutrophil,

Table 1. Demographic features of the patients according to HbA1c levels

Variables	HbA1c≤5.6 (n=35) Group 1	HbA1c 5.6-6.5 (n=65) Group 2	HbA1c≥6.5 (n=40) Group 3	p
Age, years	49±9	54±9	57±11	0.002
Male, n (%)	34 (97)	59 (91)	29 (73)	0.003
DM, n (%)	1 (3)	8 (12)	33 (83)	<0.001
HT, n (%)	9 (26)	30 (46)	25 (63)	0.006
HL, n (%)	5 (14)	6 (9)	9 (23)	0.169
Smoking, n (%)	27 (77)	50 (77)	22 (55)	0.035
Family history, n (%)	12 (34)	31 (48)	13 (33)	0.221
LVEF, %	47 (40-53)	50 (45-56)	45 (39-55)	0.207
Pain duration,min	130 (90-300)	180 (120-270)	180 (120-300)	0.379

Mean values (standard deviation) and % (n) were reported for continuous and categorical variables, respectively
DM: diabetes mellitus; HL: hyperlipidemia; HT: hypertension; LVEF: left ventricular ejection fraction

Table 2. Laboratory findings of the patients according to the HbA1c level

Variables	HbA1c≤5.6 (n=35) Group 1	HbA1c 5.6-6.5 (n=65) Group 2	HbA1c≥6.5 (n=40) Group 3	p
Glucose, mg/dL	118 (106-138)	122 (110-148)	252 (170-308)	<0.001
Creatinine, mg/dL	0.93 (0.83-0.9)	0.90 (0.86-1.04)	1.00 (0.84-1.10)	0.738
Uric acid, mg/dL	5.1 (4.3-6.2)	5.4 (4.8-6.0)	5.6 (4.4-6.5)	0.392
Amylase, U/L	65±28	62±21	57±25	0.289
TC, mg/dL	184 (164-204)	183 (156-196)	177 (152-205)	0.872
LDL-C, mg/dL	114 (102-142)	116 (89-134)	111 (73-138)	0.811
HDL-C, mg/dL	38.4±8.1	36.3±7.1	37.2±8.0	0.479
Triglyceride, mg/dL	112 (63-171)	135 (94-186)	128 (85-170)	0.287
WBC ($\times 10^9$/L)	11.1 (9.0-15.5)	11.8 (9.8-14.5)	11.3 (9.3-13.3)	0.986
Neutrophil ($\times 10^9$/L)	7.9 (6.3-12.9)	9.7 (7.2-11.2)	9.4 (6.0-10.5)	0.801
Lymphocyte ($\times 10^9$/L)	1.7 (1.3-2.6)	1.9 (1.2-2.8)	1.5 (1.1-2.4)	0.630
Hemoglobin, g/dL	14.5±1.4	14.2±1.6	13.9±2.1	0.033
Hematocrit, %	42.8±8.4	42.1±5.7	41.6±6.0	0.710
MPV, Fl	8.6 (7.7-9.1)	8.5 (7.9-9.1)	8.6 (7.8-9.4)	0.864
Platelet ($\times 10^9$/L)	238±64	243±78	251±61	0.709
RDW, %	13.0 (12.6-13.6)	13.1 (12.6-13.9)	13.5 (12.7-14.5)	0.237
HbA1c, %	5.5 (5.4-5.6)	5.9 (5.7-6.1)	7.9 (7.0-10.1)	<0.001

Mean values (standard deviation) and % (n) were reported for continuous and categorical variables, respectively
HbA1c: hemoglobin A1c; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; MPV: mean platelet volume; RDW: red cell distribution width; TC: total cholesterol; WBC: white blood cell

lymphocyte and platelet counts, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and creatinine levels were similar between all groups.

Angiographic Data

Angiographic data of the study population are presented in Table 3. Localization of infarct-related lesion (left anterior descend-

Table 3. Coronary angiography results of the patients according to the HbA1c level

Variables	HbA1c≤5.6 (n=35)	HbA1c 5.6-6.5 (n=65)	HbA1c≥6.5 (n=40)	p
The number of vessels with critical (>70%) stenosis				
Single vessel, n (%)	24 (68)	40 (61)	22 (55)	0.243
Two vessels, n (%)	10 (29)	14 (22)	10 (25)	
Three vessels, n (%)	1 (3)	11 (17)	8 (20)	
Infarct-related artery				
LAD, n (%)	20 (56)	32 (48)	21 (52)	0.751
RCA, n (%)	8 (22)	23 (35)	14 (35)	0.397
Cx, n (%)	7 (19)	9 (14)	5 (13)	0.622
LMCA, n (%)	1 (3)	2 (3)	0	0.540
TIMI blood flow				
TIMI 0, n (%)	25 (71)	38 (58)	20 (50)	0.343
TIMI 1, n (%)	1 (3)	7 (11)	3 (8)	
TIMI 2, n (%)	6 (17)	13 (20)	8 (20)	
TIMI 3, n (%)	3 (9)	7 (11)	9 (22)	
Patent IRA, n (%)	9 (26)	20 (31)	17 (43)	0.269

Cx: circumflex coronary artery; IRA: infarct-related artery; LAD: left anterior descending artery; LMCA: left main coronary artery; RCA: right coronary artery; TIMI: thrombolysis in myocardial infarction

Table 4. Coronary angiography results of diabetic patients according to the HbA1c level

Variables	HbA1c<6.5% (n=9)	HbA1c≥6.5% (n=33)	p
The number of vessels with critical (>70%) stenosis			
Single vessel, n (%)	7 (77.8)	18 (54.5)	0.301
Two vessels, n (%)	1 (11.1)	9 (27.3)	
Three vessels, n (%)	1 (11.1)	6 (18.2)	
Infarct-related artery			
LAD, n (%)	7 (77.8)	17 (51.5)	0.166
RCA, n (%)	1 (11.1)	12 (36.4)	0.154
Cx, n (%)	1 (11.1)	4 (12.1)	0.936
LMCA, n (%)	0 (0)	0 (0)	0.000
TIMI blood flow			
TIMI 0, n (%)	9 (100)	18 (54.5)	0.016
TIMI 1, n (%)	0 (0)	1 (3)	
TIMI 2, n (%)	0 (0)	8 (24.2)	
TIMI 3, n (%)	0 (0)	6 (18.2)	
Patent IRA, n (%)	0 (0)	14 (42.4)	0.016

Cx: circumflex coronary artery; IRA: Infarct-related artery; LAD: left anterior descending artery; LMCA: left main coronary artery; RCA: right coronary artery; TIMI: thrombolysis in myocardial infarction

ing artery, circumflex artery, right coronary artery) was similar between all the three groups. Number of coronary arteries with significant stenosis, TIMI flow grade, and IRA patency rates were also similar between the three groups. When patients were divided into the IRA patent and non-patent groups, in the IRA non-patent patient group, smoking rates were determined to be significantly higher (p=0.029); duration of chest pain was found to be significantly shorter (p=0.028); and LDL cholesterol levels were significantly higher (p=0.032). The MPV levels were significantly lower in the IRA patent group (p=0.014). There was no statistically significant difference between the three groups for the relation between IRA patency and HbA1c levels (p=0.260).

The patients with diabetes were also divided into two groups according to the HbA1c levels as HbA1c <6.5% (optimal blood glucose control) and HbA1c ≥6.5% (suboptimal blood glucose control) groups. Angiographic data of the diabetic patients according to their HbA1c level are showed in Table 4. According to these results, the number of vessels with critical stenosis (>70%) and the distribution of IRA were similar between both the groups. However, the rate of IRA patency was significantly higher in the suboptimal blood glucose control group compared to that in the optimal blood glucose control group (p=0.016).

The baseline demographic and laboratory findings according to the patency of IRA are demonstrated in Table 5. There were no significant differences in terms of age, incidence of hyperlipidemia, HT, DM, family history of CHD, glucose, creatinine, total cholesterol, HDL cholesterol, and triglyceride levels between the groups. In the occluded IRA group, the incidence of smoking was significantly higher compared to the patent group (p=0.029). The

Table 5. The baseline demographic and laboratory findings according to the patency of infarct-related artery

Variables	Occluded IRA (n=94)	Patent IRA (n=46)	p
Age, years	53±10	55±10	0.125
Hyperlipidemia, n (%)	15 (16)	5 (11)	0.419
Hypertension, n (%)	40 (43)	24 (52)	0.283
Diabetes mellitus, n (%)	28 (30)	14 (30)	0.937
Smoking, n (%)	72 (77)	27 (59)	0.029
Family history, n (%)	40 (43)	16 (35)	0.378
Glucose, mg/dL[Θ]	130 (112-174)	132 (110-224)	0.824
Creatinine, mg/dL	0.95±0.17	0.96±0.15	0.919
Total cholesterol, mg/dL	187±50	171±40	0.079
LDL cholesterol, mg/dL	121±44	104±32	0.032
HDL cholesterol, mg/dL	37.6±8.2	36.0±6.3	0.223
Triglyceride, mg/dL[Θ]	118 (79-162)	136 (98-188)	0.313
Uric acid, mg/dL	5.5±1.2	5.8±1.5	0.166
Amylase,U/L	64±25	56±21	0.070
HbA1c, %[Θ]	6 (5.6-6.5)	5.9 (5.7-7.3)	0.314
WBC ($\times 10^9$/L)[Θ]	12.01 (10.1-14.3)	11.05 (8.6-13.4)	0.121
Neutrophil ($\times 10^9$/L)	9.2±3.7	8.8±3.2	0.526
Lymphocyte ($\times 10^9$/L)	2.3±1.5	1.8±0.9	0.076
Hemoglobin, g/dL	14.4±1.7	14.1±1.8	0.248
Hematocrit, %	42.7±5.6	40.9±8.0	0.121
Platelet count ($\times 10^9$/L)	238±64	257±79	0.129
RDW, %[Θ]	13.1 (12.6-13.9)	13.3 (12.7-14.4)	0.109
MPV, fL	8.7±0.9	8.3±1.0	0.014
LVEF, %	47±9	49±10	0.207
Pain duration, min[Θ]	150 (90-270)	240 (120-360)	0.028

Data are expressed as mean±standard deviation
[Θ]Parameters without normal distribution
HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; MPV: mean platelet volume; RDW: red cell distribution width; WBC: white blood cell

LDL cholesterol level was also significantly higher in the occluded IRA group than the patent IRA group (121±44 mg/dL vs 104±32 mg/dL, respectively, p=0.032). In addition, MPV was significantly higher in patients within the occluded IRA group than that in the patent IRA group (8.7±0.9 fL vs 8.3±1.0 fL, respectively, p=0.014).

Table 6. Multivariate regression analysis of variables related with the patency of infarct-related artery

Variables	Possibility rate	95.0% confidence interval	p
Smoking	1.276	0.783-2.092	0.324
Mean platelet volume	0.589	0.365-0.951	0.030
Lymphocyte count	0.582	0.335-1.012	0.055
Total cholesterol	1.008	0.986-1.030	0.482
LDL cholesterol	0.978	0.952-1.004	0.101
Amylase	0.991	0.972-1.011	0.379
Pain duration	1.001	0.998-1.003	0.603

LDL: low-density lipoprotein

Multivariate regression analysis of variables related with the IRA patency is presented in Table 6. According to these results, the MPV level was detected to be an independent predictor for IRA patency (p=0.03). However, smoking (p=0.320), duration of chest pain (p=0.603), and LDL cholesterol level (p=0.101) were not independent predictors for IRA patency.

DISCUSSION

This study investigated the relation between admission HbA1c levels and IRA patency in patients with STEMI. It was found that HbA1c levels are not an independent predictor for IRA patency in these patients. Previous studies in the literature proved that coronary patency is an independent predictor for adverse events in patients with STEMI (23). Patients with patent IRA before pPCI have higher TIMI 3 flow rates after pPCI (24). In Euromax trial (25), it was proved that patients with TIMI 3 flow in IRA have better outcomes than patients with TIMI 0-2 flow in one-month follow-up. Rakowski et al. (26) showed that early IRA patency in patients with STEMI that are planned to undergo pPCI is related with better revascularization outcomes, lower mortality rates, fewer stent thrombosis, and better clinical outcomes in one-year of follow-up. Patients with TIMI flow 0 or 1 before pPCI have higher in-hospital mortality rates and major CV events (27). Patients with TIMI 0 flow before pPCI have higher short and long-term mortality rates even if TIMI 3 flow have been accomplished after pPCI (28). Previous studies showed that age, left ventricular ejection fraction, glomerular filtration rate, and Killip classes are long-term predictors for CV mortality in patients with STEMI (29). A wide range of studies have proved that HbA1c levels were related with in-hospital, long-term and short-term CV mortality, and major adverse cardiac events in patients with STEMI (30-34). Elevated levels of HbA1c are related with basic characteristics for increased CV risk. This relationship is also responsible for increased short- and long-term mortality rates. It is also known that not only patients with DM but also clinical conditions such as impaired fasting glucose, impaired glucose tolerance, and other insulin resistance conditions have very high risk for coronary artery disease development (35, 36). INTERHEART study included patients of various ethnic origin and proved that there is a strong correlation between HbA1c level and AMI incidence

independently from previously diagnosed DM (37). Lee et al. (38) conducted a study on 183 patients with DM and assessed the impact of glycemic control on occurrence of no-reflow in these patients undergoing pPCI for myocardial infarction. As a result, they found that optimal glycemic control had similar rates of no-reflow compared to the suboptimal control group. However, in this study, the rate of no-reflow was significantly higher in patients with diabetes with optimal glycemic control (HbA1c <6.5%) than those with the suboptimal group (HbA1c ≥6.5%).This result may be due to the very low number (n=9) of patients with diabetes with optimal glycemic control. Besides, elevated HbA1c levels are related with increased mortality and CV disease incidence in general population including patients with prediabetes (39, 40).

Coronary plaque rupture or erosion is considered the major cause of development of STEMI. Thrombocyte aggregation results in thrombus formation that ceases myocardial blood supply. This process causes myocardial damage. However, the actual triggering mechanism of this pathophysiologic phenomenon is unknown. Inflammation is proved to have a role in both initiation and progression of this process (41). In addition, there is a significant interaction between inflammation and atherothrombosis (42). Platelets, leukocytes, and endothelium actively participate in this process by interacting with each other. These interactions initiate autocrine and paracrine activation that leads to leukocyte migration to the vascular wall. This interaction between inflammation and thrombosis during the whole pathophysiologic process may affect IRA patency (42, 43). Previous studies have proved that proinflammatory and prothrombotic biomarkers (PLR, NLR, RDW, MPV) are directly related with IRA patency (17-19). In this study, among these biomakers including HbA1c levels, only MPV was found to be related with IRA patency in patients with STEMI before pPCI. Absence of relation between these biomarkers (except MPV) and IRA patency before pPCI may have a couple of explanations. These are different characteristics of the study population, limited number of patients, and presence of unpredictable pathophysiologic mechanisms. Brener et al. (44) showed that IRA patency before pPCI affects procedural success, in-hospital mortality, and preservation of ventricular performance. In our study, procedural success and in-hospital mortality were not evaluated. On the other hand, LVEF was measured to appraise ventricular performance. Contrary to Brener et al. (44), we found that LVEF was similar between pre-pPCI IRA patent and non-patent groups (p=0.20). Different characteristics of the study population, limited number of patients, and most importantly short chest pain-balloon time in our study may be responsible for this finding. Previous studies about patients with STEMI proved that various prothrombotic and proinflammatory biomarkers such as NLR, PLR, platelet count and reactivity, MPV, RDW, and epicardial adipose tissue thickness are related with IRA patency (17, 19, 45-49). On the scope of previous studies, we considered to evaluate the relation between HbA1c values and pre-pPCI IRA patency rates in patients with STEMI. As a result, we found similar pre-pPCI IRA patency rates in all the three HbA1c groups. Also, there was no statistically significant difference regarding HbA1c values between the IRA patent and non-patent groups. Similar to our findings, a number of studies in the literature investigating the relation between mortality and HbA1c levels in patients with AMI found no relation between IRA patency and HbA1clevels as well (32, 33). In a previous study, 374 patients with STEMI who had undergone successful pPCI were divided into three groups according to their HbA1c levels. Pre-PCITIMI flow rates were similar between groups as in our study (32). Timmer et al. (33) investigated the effect of HbA1c levels of patients with STEMI without previous DM diagnosis on short- and long-term mortality. They found that patients with higher initial blood glucose levels were associated with lesser pre-PCI TIMI 3 flow (p=0.01), while they were unable to find a difference between patients with high HbA1c levels and the control group (p=0.15) (33). In our study, we also could not find any difference regarding pre-PCI TIMI3 flow rates between patients with high HbA1c levels and the control groups.

In this study, we also found that MPV and IRA patency were independently and significantly associated with each other. Elbasan et al. (19) investigated the relation between pre-PCI IRA patency and MPV levels in 840 patients with STEMI and found that patients with MPV >9.9 fL have statistically significant lower pre-PCI TIMI 3 flow rates compared with those with MPV between 8.3 and 9.9 and MPV<8.3 fL groups. In our study, relation between MPV levels and post-pPCI TIMI flow rates was not evaluated as we assumed that the pre-pPCI TIMI flow rates could project post-pPCI rates as it is known that procedural success rates are better in pre-pPCI IRA patent patients (44). In another study conducted by Celik et al. (46), relation between MPV and post-pPCI TIMI flow rates were investigated in 306 patients with STEMI, and MPV levels were found to be lower in patients with post-pPCI TIMI 3 flow (10.9 fL vs 10.1 fL, respectively, p<0.001). However, relation between MPV and pre-pPCI IRA patency we declared in this study is consistent with other studies in the literature (19, 45, 46). Huczek et al. (50) investigated the prognostic value of MPV for angiographic reperfusion and they found that MPV is a strong, independent predictor of impaired angiographic reperfusion. In a study conducted by Kurtul et al. (51), a cut-off value of MPV >8.65 was found as a predictor of angiographic no-reflow in patients with STEMI. Moreover, in another study, Kurtul et al. (52) assessed PLR in predicting angiographic reflow in patients with STEMI and determined higher PLR in no-reflow patients compared to the normal reflow group.

There are various limitations in our study. First, retrospective single-center design may cause bias. The second most important limitation is relatively small study population. In addition to that, HbA1c levels may be affected by patients with hemoglobinopathy. Conditions such as hemolytic anemia and iron deficiency anemia may also affect test results. We did not consider these conditions.

CONCLUSION

This study showed that there is no relation between admission HbA1c levels and pre-pPCI myocardial perfusion in patients with STEMI. Besides that, data regarding increased mortality rate due to higher HbA1c levels in CHD should be reevaluated and more detailed studies are needed. Data from these studies may lead to higher threshold levels for HbA1c in patients with CHD with implementation of less aggressive treatment strategies in these patient population.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara Numune Training and Research Hospital (date: 22.02.2017, no: E-17-1248).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Design - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Supervision - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Resources - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Materials - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Data Collection and/or Processing - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Analysis and/or Interpretation - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Literature Search - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.; Writing Manuscript - A.N.A.; Critical Review - M.C.Ç., A.N.A., A.K., M.C.G., Ü.G., Y.E.Ö.

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

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Onat A, Can G, Yüksel H, Ademoğlu E, Erginel-Ünaltuna N, Kaya A, et al. Tıp dünyasının kronik hastalıklara yaklaşımına öncülük. Onat A, editör TEKHARF: Erişkinlerimizde kalp hastalıkları prevalansı, yeni koroner olaylar ve kalpten ölüm sıklığı, İstanbul: Logos yayıncılık 2017: 20-7.
2. Ezzati M, Obermeyer Z, Tzoulaki I, Mayosi BM, Elliott P, Leon DA. Contributions of risk factors and medical care to cardiovascular mortality trends. Nat Rev Cardiol 2015; 12: 508-30. [CrossRef]
3. Barchielli A, Santoro GM, Balzi D, Carrabba N, Di Bari M, Gensini GF, et al. Long-term prognosis after primary PCI in unselected patients with ST-elevation myocardial infarction. J Cardiovasc Med 2012; 13: 819-27. [CrossRef]
4. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018; 39: 119-77. [CrossRef]
5. Szuszkiewicz-Garcia MM, Davidson JA. Cardiovascular disease in diabetes mellitus: risk factors and medical therapy. Endocrinol Metab Clin North Am 2014; 43: 25-40. [CrossRef]
6. Brown A, Reynolds LR, Bruemmer D. Intensive glycemic control and cardiovascular disease: an update.Nat Rev Cardiol 2010; 7: 369-75.
7. Shan PF, Li Q, Khamaisi M, Qiang GF. Type 2 Diabetes Mellitus and Macrovascular Complications. Int J Endocrinol 2017; 2017: 4301461. [CrossRef]
8. Rensing KL, Reuwer AQ, Arsenault BJ, von der Thüsen JH, Hoekstra JB, Kastelein JJ, et al. Reducing cardiovascular disease risk in patients with type 2 diabetes and concomitant macrovascular disease: can insulin be too much of a good thing? Diabetes Obes Metab 2011; 13: 1073-87. [CrossRef]
9. Cao JJ, Hudson M, Jankowski M, Whitehouse F, Weaver WD. Relation of chronic and acute glycemic control on mortality in acute myocardial infarction with diabetes mellitus. Am J Cardiol 2005; 96: 183-86. [CrossRef]
10. Hadjadj S, Coisne D, Mauco G, Ragot S, Duengler F, Sosner P, et al. Prognostic value of admission plasma glucose and HbA1c in acute myocardial infarction. Diabet Med 2004; 21: 305-10. [CrossRef]
11. Berry C, Noble S, Gregoire J, Ibrahim R, Levesquie S, Lavoie MA, et al. Glycaemic status influences the nature and severity of coronary artery disease. Diabetologia 2010; 53: 652-8. [CrossRef]
12. Gibson CM. Has my patient achieved adequate myocardial reperfusion? Circulation 2003; 108: 504-7. [CrossRef]
13. Nammas W, Pietila M, Romppanen H, Sia J, DeBelder A, Karjalainen PP. Outcomes of poor initial TIMI flow in patients presenting with acute coronary syndrome. Scand Cardiovasc J 2017; 51: 248-54. [CrossRef]
14. Westerhout CM, Bonnefoy E, Welsh RC, Steg PG, Boutitie F, Armstrong PW. The influence of time from symptom onset and reperfusion strategy on 1-year survival in ST-elevation myocardial infarction: a pooled analysis of an early fibrinolytic strategy versus primary percutaneous coronary intervention from CAPTIM and WEST. Am Heart J 2011; 161: 283-90. [CrossRef]
15. Montalescot G, Borentain M, Payot L, Collet JP, Thomas D. Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis. JAMA 2004; 292: 362-6. [CrossRef]
16. De Luca G, Gibson CM, Gyöngyösi M, Zeymer U, Dudek D, Arntz HR, et al. Gender-related differences in outcome after ST-segment elevation myocardial infarction treated by primary angioplasty and glycoprotein IIb–IIIa inhibitors: insights from the EGYPT cooperation. J Thromb Thrombol 2010; 30: 342-6. [CrossRef]
17. Doğan M, Akyel A, Bilgin M, Erat M, Çimen T, Sunman H, et al. Can admission neutrophil to lymphocyte ratio predict infarct-related artery patency in ST-segment elevation myocardial infarction. Clin Appl Thromb Hemost 2015; 21: 172-6. [CrossRef]
18. Şahin DY, Gür M, Elbasan Z, Yıldız A, Kaya Z, İçen YK, et al. Predictors of preinterventional patency of infarct-related artery in patients with ST-segment elevation myocardial infarction: Importance of neutrophil to lymphocyte ratio and uric acid level. Exp Clin Cardiol 2013; 18: e77.
19. Elbasan Z, Gür M, Şahin DY, Kuloglu O, Icen YK, Turkoglu C, et al. Association of mean platelet volume and pre-and postinterventional flow with infarct-related artery in ST-segment elevation myocardial infarction. Angiology 2013; 64: 440-6. [CrossRef]
20. Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33: 62. [CrossRef]
21. Members ATF, Steg PG, James SK, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). Eur Heart J 2012; 33: 2569-619. [CrossRef]
22. Bailleul C, Puymirat E, Aissaoui N, Schiele F, Ducrocq G, Coste P, et al. Factors associated with infarct-related artery patency before primary percutaneous coronary intervention for st-elevation myocardial infarction (from the FAST-MI 2010 registry). Am J Cardiol 2016; 117: 17-21. [CrossRef]
23. Brener SJ, Mehran R, Brodie BR, Guagliumi G, Witzenbichler B, Cristea E, et al. Predictors and Implications of Coronary Infarct Artery Pate ncy at Initial Angiography in Patients With Acute Myocardial Infarction (from the CADILLAC and HORIZONS-AMI Trials). Am J Cardiol 2011; 108: 918-23. [CrossRef]
24. Mehta RH, Harjai KJ, Cox D, Stone GW, Brodie B, Boura J, et al. Clinical and angiographic correlates and outcomes of suboptimal coronary flow in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention. J Am Coll Cardiol 2003; 42: 1739-46. [CrossRef]
25. Rakowski T, Dudek D, van 't Hof A, Ten Berg J, Soulat L, Zeymer U, et al. Impact of acute infarct-related artery patency before percutaneous coronary intervention on 30-day outcomes in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention in the EUROMAX trial. Eur Heart J Acute Cardiovasc Care 2018; 7: 514-21. [CrossRef]

26. Rakowski T, Dudek D, Dziewierz A, Yu J, Witzenbichler B, Guagliumi G, et al. Impact of infarct-related artery patency before primary PCI on outcome in patients with ST-segment elevation myocardial infarction: the HORIZONS-AMI trial. Euro Intervention 2013; 8: 1307-14. [CrossRef]
27. Wu J, Pride YB, Frederick PD, Gibson CM. Association of initial thrombolysis in myocardial infarction flow grade with mortality among patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a National Registry of Myocardial Infarction-5 (NRMI-5) analysis. Am Heart J 2011; 162: 178-83. [CrossRef]
28. Valgimigli M, Campo G, Malagutti P, Anselmi M, Bolognese L, Ribichini F, et al. Persistent coronary no flow after wire insertion is an early and readily available mortality risk factor despite successful mechanical intervention in acute myocardial infarction: a pooled analysis from the strategy (single high-dose bolus tirofiban and sirolimus-eluting stent versus abciximab and bare-metal stent in acute myocardial infarction) and multistrategy (multicenter evaluation of single high-dose bolus tirofiban versus abciximab with sirolimus-eluting stent or bare-metal stent in acute myocardial infarction study) trials. JACC 2011; 4: 51-62.
29. Yao H, Ekou A, Hadeou A, N'Djessan JJ, Kouamé I, N'Guetta R. Medium and long-term follow-up after ST segment elevation myocardial infarction in a sub-Saharan Africa population:a prospective cohort study. BMC Cardiovasc Disord 2019; 19: 65-71. [CrossRef]
30. Tenerz Å, Nilsson G, Forberg R, Ohrvik J, Malmberg K, Berne C, et al. Basal glucometabolic status has an impact on long-term prognosis following an acute myocardial infarction in non-diabetic patients. J Intern Med 2003; 254: 494-503. [CrossRef]
31. Tian L, Zhu J, Liu L, Liang Y, Li J, Yang Y. Hemoglobin A1c and short-term outcomes in patients with acute myocardial infarction undergoing primary angioplasty: an observational multicenter study. Coron Artery Dis 2013; 24: 16-22. [CrossRef]
32. Cicek G, Uyarel H, Ergelen M, Ayhan E, Abanonu GB, Eren M, et al. Hemoglobin A1c as a prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction. Coron Artery Dis 2011; 22: 131-7. [CrossRef]
33. Timmer JR, Hoekstra M, Nijsten MW, van der Horst IC, Ottervanger JP, Slingerland RJ, et al. Prognostic value of admission glycosylated hemoglobin and glucose in nondiabetic patients with ST-segment–elevation myocardial infarction treated with percutaneous coronary intervention. Circulation 2011; 124: 704-11. [CrossRef]
34. Pusuroglu H, Akgul O, Cakmak HA, Erturk M, Surgit O, Celik O, et al. Long-term prognostic value of admission haemoglobin A1c (HbA1c) levels in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Postepy Kardiol Interwencyjnej 2014; 10: 166. [CrossRef]
35. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. Ann Intern Med 2014; 141: 413-20. [CrossRef]
36. Lee CH, Lee SW, Park SW. Diabetes and subclinical coronary atherosclerosis. Diabetes Metab J 2018; 42: 355-63. [CrossRef]
37. Gerstein H, Islam S, Anand S, Almahmeed W, Damasceno A, Dans A, et al. Dysglycaemia and the risk of acute myocardial infarction in multiple ethnic groups: an analysis of 15,780 patients from the INTERHEART study. Diabetologia 2010; 53: 2509-17. [CrossRef]
38. Lee CH, Teo SG, Hong E, Wong HB, Low A, Sutandar A, et al. Impact of glycemic control on occurrence of no-reflow and 30-day outcomes in diabetic patients undergoing primary angioplasty for myocardial infarction. J Invasive Cardiol 2005; 17: 422-6.
39. Eskesen K, Jensen M, Galatius S, Vestergaard H, Hildebrandt P, Marott JL, et al. Glycated haemoglobin and the risk of cardiovascular disease, diabetes and all-cause mortality in the Copenhagen City Heart Study. J Intern Med 2013; 273: 94-101. [CrossRef]
40. Selvin E, Steffes MW, Zhu H, Matsushita K, Wagenknecht L, Pankow J, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. N Engl J Med 2010; 362: 800-11. [CrossRef]
41. Wolf D, Ley K. Immunity and Inflammation in Atherosclerosis. Circ Res 2019; 124: 315-27. [CrossRef]
42. Fuentes Q E, Fuentes Q F, Andrés V, Pello OM, Font de Mora J, Palomo GI. Role of platelets as mediators that link inflammation and thrombosis in atherosclerosis. Platelets 2013; 24: 255-62. [CrossRef]
43. Maseri A, Fuster V. Is there a vulnerable plaque? Circulation 2003; 107: 2068-71. [CrossRef]
44. Brener SJ, Mehran R, Brodie BR, Guagliumi G, Witzenbichler B, Cristea E, et al. Predictors and implications of coronary infarct artery patency at initial angiography in patients with acute myocardial infarction (from the CADILLAC and HORIZONS-AMI Trials). Am J Cardiol 2011; 108: 918-23. [CrossRef]
45. Breet NJ, van Werkum JW, Bouman HJ, Kelder JC, Hackeng CM, ten Berg JM. The relationship between platelet reactivity and infarct-related artery patency in patients presenting with a ST-elevation myocardial infarction. Thromb Haemost 2011; 105: 331-6. [CrossRef]
46. Celik T, Kaya MG, Akpek M, Gunebakmaz O, Balta S, Sarli B, et al. Predictive value of admission platelet volume indices for in-hospital major adverse cardiovascular events in acute ST-segment elevation myocardial infarction. Angiology 2015; 66: 155-62. [CrossRef]
47. Sen F, Yilmaz S, Balci KG, Gül M, Balcı MM, Akboga MK, et al. The relationship between epicardial adipose tissue thickness and infarct-related artery patency in patients with ST-segment elevation myocardial infarction. Angiology 2016; 67: 281-6. [CrossRef]
48. Yayla Ç, Akboğa MK, Canpolat U, Akyel A, Yayla KG, Doğan M, et al. Platelet to lymphocyte ratio can be a predictor of infarct-related artery patency in patients with ST-segment elevation myocardial infarction. Angiology 2015; 66: 831-6. [CrossRef]
49. Akboga MK, Yayla C, Yilmaz S, Sen F, Balcı KG, Ozcan F, et al. Increased red cell distribution width predicts occlusion of the infarct-related artery in STEMI. Scand Cardiovasc J 2016; 50: 114-8. [CrossRef]
50. Huczek Z, Kochman J, Filipak KJ, Horszczaruk GJ, Grabowski M, Piatkowski R , et al. Mean platelet volüme on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005; 46: 284-90. [CrossRef]
51. Kurtul A, Açıkgöz SK. Usefulness of mean platelet volume to lymphocyte ratio for predicting angiographic no-reflow and short term prognosis after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Am J Cardiol 2017; 120: 534-41. [CrossRef]
52. Kurtul A, Yarlıoglues M, Murat SN, Ergun G, Duran M, Kasapkara HA, et al. Usefulness of platelet to lymphocyte ratio in predicting angiographic reflow after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction. Am J Cardiol 2014; 114: 342-7. [CrossRef]