Impact of High-Degree Atrioventricular Block on No-Reflow Phenomenon and Prognosis in Patients with St-Segment Elevation Myocardial Infarction

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ABSTRACT

Introduction: Although it has been established that high-degree atrioventricular block (HAVB) is associated with mortality in the course of ST segment elevation myocardial infarction (STEMI), the mechanisms by which this AV block cause mortality are not yet fully understood. In this study we aimed: (i) to investigate the relationship between HAVB and no-reflow, which has been repeatedly shown to be associated with both short- and long-term mortality; (ii) to determine the effect of both HAVB and no-reflow on in-hospital and long-term mortality.

Patients and Methods: A total of 1.217 patients who underwent primary percutaneous coronary intervention (pPCI) were divided into two groups, according to HAVB development, and were further divided according to no-reflow development. Independent predictors of no-reflow were investigated. Furthermore, patients were compared in terms of in-hospital and long-term mortality.

Results: In the present study, 47 patients (3.8%) suffered from HAVB and 150 patients (12.3%) had no-reflow. HAVB was an independent predictor of no-reflow [odds ratio (OR): 3.127, 95% confidence interval (CI): 1.215-9.056; p= 0.006]. In survival analysis, both HAVB and no-reflow were associated with in-hospital (19.1% vs. 3.2%; p< 0.001 and 10.7% vs. 2.9%; p< 0.001, respectively) and long-term (15.7% vs. 6.2%; p= 0.037 and 14.1% vs. 5.5%; p< 0.001, respectively) mortality.

Conclusion: To our knowledge, this is the first study in the literature to examine the effect of HAVB on reperfusion success. In this study, we found that HAVB emerged with STEMI is associated with long-term mortality and to short-term mortality. Also HAVB was an independent predictor of no-reflow, and patients who had no-reflow had a worse prognosis both in short- and long-term follow-up.

Key Words: High grade AV block; ST segment elevation myocardial infarction; no-reflow

St-Segment Yükselmeli Miyokart İnfarktüslü Hastalarda Yüksek Dereceli Atriyoventriküler Bloğun No-reflow Fenomenine ve Prognoza Etkisi

ÖZET

Giriş: ST segment yükselmeli miyokart infarktüsü (STEMİ) seyrinde yüksek dereceli atriyoventriküler bloğun (HAVB) mortalite ile ilişkili olduğu tespit edilmiş olsa da AV bloğunun mortaliteye hangi mekanizmalarla neden olduğu, net olarak ortaya konulmamıştır. Bu çalışmada, (i) HAVB ile hem kısa hem de uzun dönem mortalite ile ilişkili olduğu defalarca gösterilen no-reflow arasındaki ilişkiyi (ii) hem HAVB hem de no-reflow'un hastane içi ve uzun dönem mortaliteye etkisini araştırmayı amaçladık.

Hastalar ve Yöntem: Primer perkütan koroner girişim (pPCI) yapılan toplam 1217 hasta, HAVB gelişip gelişmemesine, daha sonra da no-reflow gelişip gelişmemesine göre iki gruba ayrıldı. No-reflow'un bağımsız prediktörleri araştırıldı. Son olarak da hastalar, hastane içi ve uzun dönem mortalite açısından karşılaştırıldı.

Bulgular: Bu çalışmada, 47 (%3.8) hastada HAVB, 150 (%12.3) hastada no-reflow izlendi. HAVB, no-reflow'un bağımsız bir prediktörü olarak saptandı (OR: 3.127, %95 CI: 1.215-9.056; p= 0.006). Sağkalım analizinde HAVB ve no-reflow'da hastane içi mortalite (sırasıyla %19.1'e karşı %3.2; p< 0.001 ve %10.7'ye karşı %2.9; p< 0.001) ve uzun dönem mortalite (sırasıyla %15.7'ye karşı %6.2; p= 0.037 ve %14.1'e karşı %5.5; p< 0.001) daha yüksek olarak izlendi.

Sonuç: Bu çalışmada, STEMİ ile ortaya çıkan HAVB'nin, kısa döneme ek olarak, uzun dönem mortalite ile de ilişkili olduğu tespit edildi. HAVB ile sağkalımla ileri derecede korelasyonu olan reperfüzyon başarısının ilişkisini gösteren bu ilk çalışmada, HAVB'nin no-reflow için bağımsız bir prediktör olduğunu ve no-reflow'u olan hastaların hem kısa hem de uzun dönem izlemlerinde kötü prognoza sahip olduğunu ortaya koyduk.

Anahtar Kelimeler: Yüksek dereceli atriyoventriküler blok; ST segment yükselmeli miyokart infarktüsü; no-reflow

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INTRODUCTION

Electrical conduction abnormalities are one of the major complications of acute ST segment elevation myocardial infarction (STEMI). Autonomic imbalance or ischemia and necrosis of the conduction system are known as the most likely mechanisms of STEMI. High-degree atrioventricular block (HAVB), defined as the presence of Mobitz type II second-degree or third-degree AV block, is a dominant manifestation of AV conduction disturbance, with an incidence of 1.5%-6.9%[1,2]. Although primary percutaneous coronary intervention (pPCI) can ameliorate AV blocks complicating acute STEMI, HAVB continues to be associated with ominous outcomes, such as in-hospital death[3-5].

In the setting of pPCI, no-reflow is defined as suboptimal myocardial reperfusion through a part of the coronary circulation without angiographic evidence of mechanical vessel obstruction[6]. No-reflow is associated with lower left ventricular ejection fraction (LVEF), adverse left ventricular remodeling, increased number of mechanical complications, and short- and long-term mortality[7-9].

Although many studies previously performed have focused on association between HAVB and mortality, the mechanism by which the AV block causes mortality has not yet been clearly elucidated. In this study, we aimed to determine the impact of HAVB on reperfusion success, and the effect of both HAVB and no-reflow on in-hospital and long-term mortality.

PATIENTS and METHODS

Study Population

A total of 1.303 patients with STEMI who underwent pPCI from January 2011 to June 2015 were retrospectively enrolled in this study. STEMI was defined based on the following criteria: a typical increase or decrease in cardiac biomarkers; ongoing ischemic symptoms (within 12 h of presentation); newly-developed left bundle-branch block pattern, or a new ST elevation in two or more contiguous leads, with readings of at least 0.2 mV in leads V1, V2, and V3, or at least 0.1 mV in the remaining leads; or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality[10]. HAVB was defined as the presence of Mobitz type II second-degree or third-degree AV block accompanied by symptoms and signs of low cardiac output. A temporary pacemaker was applied to all patients with HAVB present and being symptomatic, as soon as possible. A total of 86 patients treated noninvasively, patients under treatment of hemodialysis and having electrolyte imbalance, and patients whose final diagnosis on discharge was other than STEMI (e.g., myocarditis, Kounis syndrome, or Takotusubo cardiomyopathy), were excluded from the study. A total of the remaining 1.217 patients who were all treated with pPCI constituted the study population. Long-term follow-up data was obtained from hospital records and phone interviews. For patients unable to be reached, we gathered information from the National Institute of Statistics and the Registrar of Birth Records to determine whether or not they were deceased.

The study protocol was reviewed and approved by the Local Ethics Committee of the Kafkas University and was conducted in accordance with the Declaration of Helsinki.

Data Collections

Baseline clinical and demographic characteristics and patients' medical history data were obtained from the hospital records. Complete blood count and blood biochemical parameters were measured in all patients on admission to the hospital and prior to pPCI. Blood samples were retested for troponin T and creatine kinase myocardial band (CK-MB) every six hours, until peak levels were detected. Afterwards, these tests, along with hemograms and creatinine tests, were repeated daily. Estimated glomerular filtration rate (eGFR) was determined using Cockroft-Gault formula from blood samples that were obtained on admission. LVEF was defined as the post-procedural ejection fraction, and was assessed using a modified Simpson's method.

Angiographic Analysis

The standard Judkins percutaneous transfemoral technique was used for all patients who were treated with pPCI by experienced interventional cardiologists. Coronary angiograms were recorded in digital media for quantitative analysis (Dicomviewer; MedCom GmbH, Darmstadt, Germany). Digital angiograms were analyzed by two independent and experienced interventional cardiologists, who were blinded to all data. Patients' Syntax scores were calculated using SS Calculator, version 2.1[11]. Acute transient or persistent coronary flow reduction [final thrombolysis in myocardial infarction (TIMI) flow grade < 3 or final myocardial blush grade (MBG) < 2] at the target vessel lesion in the absence of spasm, trombus, dissection, and/or significant residual stenosis was defined as epicardial no-reflow[12].

Statistical Analysis

The statistical analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL). With respect to data distribution and normality, the mean (± standard deviation) or median (0.25-0.75 percentiles) was used to express continuous variables, and a t-test or Mann-Whitney U-test was conducted to compare variables. The categorical variables were presented as numbers (percentages) and compared using Fisher's Exact test or an $\chi 2$-test. Multivariable logistic regression analyses were performed to identify the independent predictors of no-reflow, using variables that showed statistically significant association with no-reflow in the univariate analyses. Survival curves were calculated using the Kaplan-Meier method. Statistical significance was assessed using log-rank tests. A p-value < 0.05 indicated statistical significance.

RESULTS

The study population consisted of 1.217 STEMI patients (mean age: 56 ± 12.3 years; 81.5% were males) who underwent pPCI. HAVB was observed in 3.86% (n= 47) of the study population. Demographic, clinical, laboratory, and coronary angiographic characteristics of all patients, patients with HAVB and without HAVB, are listed in Table 1. Heart rate was significantly lower in patients with HAVB as compared with patients without HAVB (35 ± 5.3 vs. 79 ± 13.9; p< 0.001). No-reflow was significantly more frequent in patients with HAVB than in those patients without (11.7% vs. 23.4%; p< 0.001). Patients with HAVB were older, had higher level of C-reactive protein (CRP), and higher percentage of infarct related artery (IRA) of RCA than did those patients without HAVB. Furthermore, compared to patients without HAVB, patients with HAVB had lower systolic blood pressure and lower levels of hemoglobin, albumin, and eGFR; a longer stent length and more frequent ventricular arrhythmia. There was no difference between patients with and without HAVB in terms of infarct size (detected by CK-MB), coronary artery disease (CAD) severity (determined by Syntax score), Killip class on admission, B-type natriuretic peptide, LVEF, and total ischemia time.

123 patients (9.9%) died during a mean follow-up of 43.3 months. The rate of in-hospital mortality was significantly higher in those patients with HAVB than in those patients without HAVB (n= 9, 19.1% vs. n= 38, 3.2%; p< 0.001). The Kaplan-Meier survival curve of in-hospital mortality is shown in Figure 1A. Long-term mortality rate of survivors who discharged from the hospital (n= 38 patients with HAVB, n= 1132 patients without HAVB) was still higher in patients with HAVB than those without (n= 6, 15.7% vs. n= 70, 6.2%; p= 0.037 Figure 1B).

When the relationship between no-reflow in patients with HAVB and other variables was examined; it was seen that HAVB was more frequent in patients with no-reflow than in those patients without no-reflow. Patients with no-reflow were older, had a more frequent history of diabetes mellitus (DM) and hyperlipidemia, and had a higher percentage of smoking, compared to those patients without no-reflow. Compared to patients without no-reflow, patients with no-reflow had a higher Killip class on admission; higher white blood cell (WBC) and neutrophil count; lower lymphocyte count; higher level of peak CK-MB and troponin, CRP, B-type natriuretic peptide (BNP), and fasting blood glucose (FBG); and lower hemoglobin, serum albumin, eGFR, and LVEF. Furthermore, patients with no-reflow had longer and smaller stent size; higher basal Syntax score; longer total ischemic time; more frequent thrombus grade ≥ 3 and proximal/ostial lesion location than did those patients without no-reflow (Table 2).

Multivariate regression analysis was used to determine the independent predictors of no-reflow by using parameters that were found to be associated with no-reflow in the univariate analysis (Table 3). HAVB (OR: 3.127, 95% CI: 1.215-9.056; p= 0.006), neutrophil-to-lymphocyte ratio (OR: 1.048, 95% CI: 1.009-1.087; p= 0.015), CRP (OR: 1.102, 95% CI: 1.008-1.202; p= 0.027), LVEF (OR: 0.954, 95% CI: 0.898-0.976; p< 0.001), total ischemia time (OR: 1.007, 95% CI: 1.005-1.009; p< 0.001), thrombus grade ≥ 3 (OR: 2.317 95% CI: 1.284-4.179; p= 0.005), stent length (per 1 mm, OR: 1.054, 95% CI: 1.032-1.091; p< 0.001), and stent diameter (per 1 mm, OR: 2.128, 95% CI: 1.186-4.354; p= 0.011) were found to be independent predictors of no-reflow.

The rate of in-hospital mortality was significantly higher in patients with no-reflow than in those patients without no-reflow (n= 16, 10.7% vs. n= 31, 2.9%; p< 0.001). The Kaplan-Meier survival curve of in-hospital mortality is shown in Figure 2A. The rate of long-term mortality [the rate among the survivors (n= 134 patients with no-reflow, n= 1031 patients without no-reflow)] beyond discharge was still significantly higher for no-reflow patients compared to patients without no-reflow (n= 19, 14.1% vs. n= 57, 5.5%; p< 0.001 Figure 2B).

DISCUSSION

In the present study, we focused on the potential relationship between HAVB and the development of no-reflow in patients undergoing pPCI for STEMI. Our study demonstrated that STEMI patients with no-reflow had a higher frequency of HAVB. HAVB was shown to be an independent predictor of no-reflow development during pPCI, and patients who had both HAVB and/or no-reflow had a worse prognosis for mortality both in-hospital and in long-term follow up.

HAVB with a slow escape rhythm is a potentially fatal event in the setting of STEMI if not detected and treated. Although a significant portion of HAVB is transient, rarely may it progress to irreversible and symptomatic block. To date, several clinical parameters related to the development of HAVB have been established in STEMI patients. Consistent with the results of previous studies, we found that older age, infarct-related arteries of RCA, and reduced eGFR were associated with increased likelihood of HAVB development[1,4,5]. In accordance with previous studies, LVEF, infarct size, total ischemic time, and CAD severity (in this study determined by Syntax) were not different in patients with and without HAVB[1,5,13]. In the present study, we also observed that patients with HAVB had a reduced level of hemoglobin. Although there is no definitive relationship between anemia alone and HAVB, anemia could probably facilitate HAVB in STEMI patients through reduction in oxygen presentation and emergence of deeper tissue hypoxia[14].

A significant number of previous studies have shown that HAVB is associated with short-term mortality, but the results of long-term mortality seem contradictory[1,4,5,13,15]. In our study, which had one of the longest follow-ups to date, HAVB was associated with both in-hospital and long-term mortality. Although many studies have focused on the relationship between HAVB and mortality, the mechanism by which HAVB causes

Table 1. Demographic, clinical, and laboratory characteristics of all patients; patients with and without HAVB, with p-value

		HAVB		
	All patients (n= 1217)	**Patients without HAVB n= 1170**	**Patients with HAVB n= 47**	**p**
Age	56 ± 12.3	56 12	61 ± 12.2	0.012
Male gender, n (%)	992 (81.5)	953 (81.5)	39 (83.0)	0.792
Diabetes, n (%)	280 (23.0)	268 (22.9)	12 (25.5)	0.675
Hypertension, n (%)	491 (40.3)	466 (39.8)	25 (53.2)	0.067
Hyperlipidemia, n (%)	538 (44.2)	518 (44.3)	20 (42.6)	0.816
COPD, n (%)	59 (4.8)	56 (4.8)	3 (6.4)	0.617
PAD, n (%)	205 (16.8)	198 (16.9)	7 (14.9)	0.716
Family history of CAD, n (%)	280 (23.0)	273 (23.3)	7 (14.9)	0.178
Smoking, n (%)	663 (54.5)	636 (54.4)	27 (57.4)	0.677
ASA, n (%)	25 (2.1)	24 (2.1)	1 (2.1)	0.971
b-Blocker, n (%)	86 (7.1)	82 (7.0)	4 (8.5)	0.694
ACEI/ARB, n (%)	238 (19.6)	230 (19.7)	8 (17.0)	0.655
Statin, n (%)	213 (17.5)	208 (17.8)	5 (10.6)	0.207
Insulin, n (%)	82 (6.7)	77 (6.6)	5 (10.6)	0.277
Arrest on admission	30 (2.5)	28 (2.4)	2 (4.3)	0.420
Killip class > 1 on admission (%)	195 (16.0)	186 (15.9)	9 (19.1)	0.551
Systolic blood pressure, mmHg	132 ± 31.7	132 ± 30.9	118 ± 45.5	0.012
Heart rate, bpm	77 ± 16.1	79 ± 13.9	35 ± 5.3	< 0.001
Hemoglobin (g/dL)	13.7 ± 1.8	13.7 ± 1.8	12.9 ± 2.0	0.009
WBC count (/1000)	12.329 ± 3.9	12.301 ± 3.8	13.020 ± 5.4	0.587
Platelet count (10.000/microliter)	258 ± 68.0	259 ± 67.9	249 ± 70.9	0.301
Neutrophil count (/1000)	9.573 ± 3.7	9.556 ± 3.6	9.991 ± 4.8	0.794
Lymphocyte count (/1000)	1.7 1.2-2.4	1.7 1.2-2.4	1.7 1.2-2.3	0.978
Neutrophil-to-lymphocyte ratio	5.3 3.4-8.2	5.3 3.4-8.2	4.9 3.5-7.3	0.639
FBG on admission (mg/dL)	127.0 105.0-170.5	127.0 105.0-170.0	139.0 109.0-203.0	0.131
C-Reactive protein (mg/dL)	10.0 5.6-17.6	9.9 5.6-17.3	12.1 7.8-24.1	0.045
Serum albumin (g/dL)	3.74 ± 0.48	3.75 ± 0.48	3.51 ± 0.42	< 0.001
Estimated glomerular filtration rate	88.27 ± 25.56	88.73 ± 25.29	76.94 ± 29.71	0.016
Peak creatine kinase MB (ng/mL)	179.0 101.5-320.0	176.0 101.0-316.0	234.0 144.0-360.0	0.073
Peak troponin I (ng/mL)	82.2 37.8-187.0	81.4 37.0-186.9	94.0 59.8-223.5	0.166
B-type natriuretic peptide pg/mL	73.7 35.8-137.1	72.0 35.0-134.6	87.0 49.9-174.3	0.113
Left ventricular ejection fraction (%)	46.70 8.33	46.71 8.36	46.46 7.80	0.771
Total ischemia time, min	179.0 115.0-270.0	178.5 115.0-270.0	190.0 112.0-315.0	0.713
Infarct-related artery, n (%)				
LAD	634 (52.1)	633 (54.1)	1 (2.1)	< 0.001
Cx	151 (12.4)	149 (12.7)	2 (4.3)	
RCA	415 (34.1)	371 (31.7)	44 (93.6)	
Other coronaries (diagonal etc.)	17 (1.4)	17 (1.5)	0 (0.0)	

HAVB: High degree atrioventricular block, COPD: Chronic obstructive pulmonary disease, PAD: Peripheral arterial disease, CAD: Coronary artery disease, ASA: Acetylsalicylic acid, ACEI/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker, WBC: White blood cell, FBG: Fasting blood glucose, IRA: Infarct-related artery.

Table 1. Demographic, clinical, and laboratory characteristics of all patients; patients with and without HAVB, with p-value (continues)

		HAVB		
	All patients (n= 1217)	**Patients without HAVB n= 1170**	**Patients with HAVB n= 47**	**p**
Proximal/ostial lesion for IRA, n (%)	702 (57.7)	677 (57.9)	25 (53.2)	0.525
Stent length, mm	21.85 ± 9.1	21.71 8.90	25.65 ± 12.7	0.003
Stent diameter, mm	3.11 ± 0.4	3.10 0.36	3.20 ± 0.5	0.146
Thrombus grade ≥ 3, n (%)	804 (66.1)	767 (65.6)	37 (78.7)	0.062
No-reflow	150 (12.3)	131 (11.7)	19 (23.4)	< 0.001
Ventricular tachycardia/fibrillation, n (%)	67 (5.5)	61 (5.20)	6 (12.8)	0.026
Basal syntax score	16.63 ± 4.5	16.61 ± 4.5	17.27 ± 3.8	0.107

HAVB: High degree atrioventricular block, COPD: Chronic obstructive pulmonary disease, PAD: Peripheral arterial disease; CAD: Coronary artery disease, ASA: Acetylsalicylic acid, ACEI/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker, WBC: White blood cell, FBG: Fasting blood glucose, IRA: Infarct-related artery.

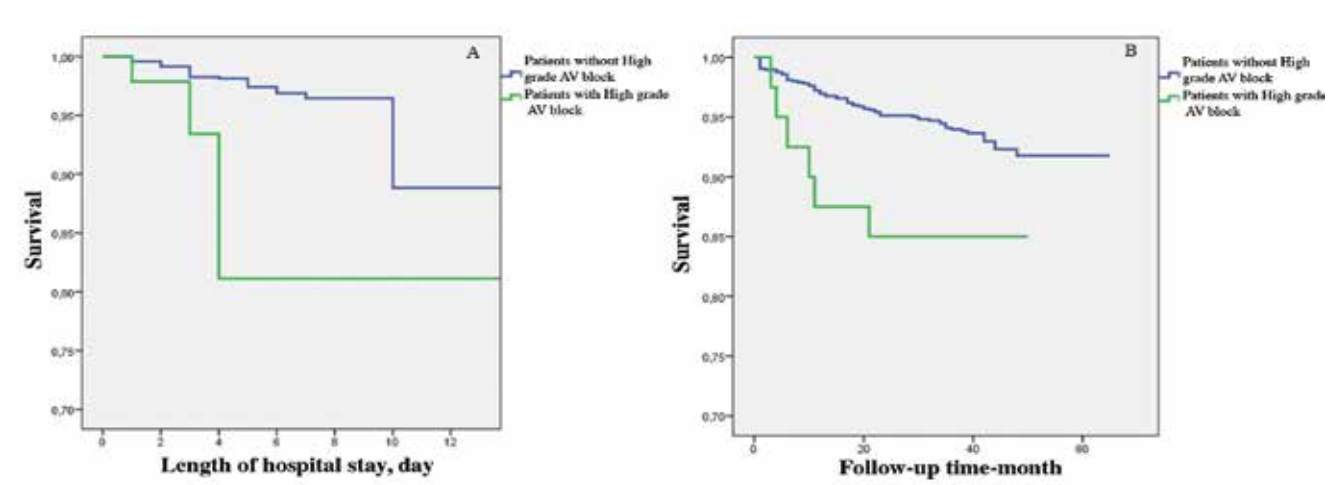

Figure 1. Kaplan-Meier survival analysis of in hospital (A) and long-term mortality (B) in patients with and without high grade atrioventricular block.

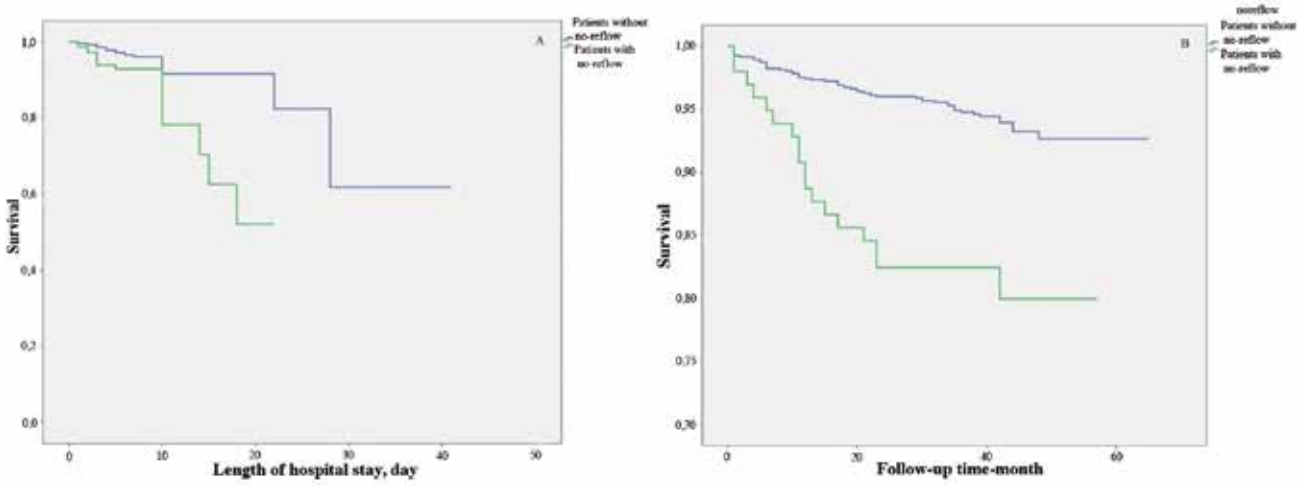

Figure 2. Kaplan-Meier survival analysis of in hospital (A) and long-term mortality (B) in patients with and without no-reflow.

Table 2. Demographic, clinical, and laboratory characteristics of all patients; patients with and without no-reflow, with p-value

	No-reflow		
	(–); n= 1067	**(+); n= 150**	**p**
Age	56 ± 12	61 ± 13	< 0.001
Female gender, n (%)	874.0 (81.9)	118.0 (78.7)	0.338
Diabetes, n (%)	236.0 (22.1)	44.0 (29.3)	0.049
Hypertension, n (%)	415.0 (38.9)	76.0 (50.7)	0.006
Hyperlipidemia, n (%)	483.0 (45.3)	55.0 (36.7)	0.047
COPD, n (%)	49.0 (4.6)	10.0 (6.7)	0.268
PAD, n (%)	172.0 (16.1)	33.0 (22.0)	0.072
Family history of CAD, n (%)	250.0 (23.4)	30.0 (20.0)	0.350
Smoking, n (%)	594.0 (55.7)	69.0 (46.0)	0.026
ASA, n (%)	23.0 (2.2)	2.0 (1.3)	0.506
b-Blocker, n (%)	77.0 (7.2)	9.0 (6.0)	0.586
ACEI/ARB, n (%)	208.0 (19.5)	30.0 (20.0)	0.884
Statin, n (%)	204.0 (19.1)	9.0 (6.0)	< 0.001
Insulin, n (%)	70.0 (6.6)	12.0 (8.0)	0.510
Arrest on admission	23.0 (2.2)	7.0 (4.7)	0.063
Killip class > 1 on admission (%)	157.0 (14.7)	38.0 (25.3)	0.001
Systolic blood pressure, mmHg	131 ± 30	138 ± 43	0.063
Heart rate, bpm	77 ± 15	76 ± 21	0.976
Hemoglobin (g/dL)	13.7 ± 1.8	13.5 ± 2.0	0.131
WBC count (/1000)	12.174 ± 3.752	13.434 ± 4.394	< 0.001
Platelet count (10000/microliter)	258 ± 68	258 ± 71	0.879
Neutrophil count (/1000)	9.390 ± 3.570	10.872 ± 3.967	< 0.001
Lymphocyte count (/1000)	1.800 1.264-2.400	1.500 1.000-2.100	0.001
Neutrophil-to-lymphocyte ratio	5.07 3.35-7.82	7.34 4.17-11.00	< 0.001
FBG on admission (mg/dL)	150.10 ± 75.70	167.59 ± 84.97	< 0.001
C-Reactive protein (mg/dL)	9.50 5.33-16.50	16.50 7.74-31.20	< 0.001
Serum albumin (g/dL)	3.76 ± 0.48	3.65 ± 0.48	0.001
Estimated glomerular filtration rate	89.32 ± 25.18	80.84 ± 27.08	< 0.001
Peak creatine kinase MB (ng/mL)	163.0 94.0-287.0	342.50 212.00-467.00	< 0.001
Peak troponin I (ng/mL)	77.00 34.00-165.00	181.82 77.00-276.00	< 0.001
B-type natriuretic peptide pg/mL	65.35 33.40-121.30	133.50 85.85-279.80	< 0.001
Left ventricular ejection fraction (%)	47.65 ± 8.03	40.18 ± 7.44	< 0.001
Total ischemia time, min	170.0 110.0-252.0	301.5 198.0-395.0	< 0.001
Infarct-related LAD artery, n (%)			
LAD	558.0 (52.3)	76.0 (50.7)	0.808
Cx	132.0 (12.4)	19.0 (12.7)	
RCA	360.0 (33.7)	55.0 (36.7)	
Other coronaries (diagonal etc.)	17.0 (1.6)	0.0 (0.0)	

COPD: Chronic obstructive pulmonary disease, PAD: Peripheral arterial disease, CAD: Coronary artery disease, ASA: Acetylsalicylic acid, ACEI/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker, WBC: White blood cell, FBG: Fasting blood glucose,IRA: Infarct-related artery.

Table 2. Demographic, clinical, and laboratory characteristics of all patients; patients with and without no-reflow, with p-value (continues)

	No-reflow		
	(–); n= 1067	**(+); n= 150**	**p**
Proximal/ostial lesion for IRA, n (%)	590.0 (55.3)	112.0 (74.7)	< 0.001
Stent length, mm	21.02 ± 8.17	28.06 ± 12.57	< 0.001
Stent diameter, mm	3.09 ± 0.34	3.23 ± 0.50	0.011
Thrombus grade ≥ 3, n (%)	672 (63.0)	132 (88.0)	< 0.001
Basal syntax score	16.37 ± 4.54	18.53 ± 3.86	< 0.001
High degree AV block	28.00 (2.6)	19.00 (12.7)	< 0.001

COPD: Chronic obstructive pulmonary disease, PAD: Peripheral arterial disease, CAD: Coronary artery disease, ASA: Acetylsalicylic acid, ACEI/ARB: Angiotensin converting enzyme inhibitor/angiotensin receptor blocker, WBC: White blood cell, FBG: Fasting blood glucose, IRA: Infarct-related artery.

Table 3. Univariate and multivariate logistic regression analysis of demographic, clinical, laboratory, and coronary angiographic characteristics for no-reflow prediction

	Univariate analysis of no-reflow			Multivariate analysis of no-reflow		
	Odds ratio	**95% CI**	**p**	**Odds ratio**	**95% CI**	**p**
High Grade AV block	5.382	2.924-9.908	< 0.001	3.127	1.215-9.056	0.006
Neutrophil-to-lymphocyte ratio	1.076	1.044-1.108	< 0.001	1.048	1.009-1.087	0.015
C-reactive protein	1.039	1.028-1.050	< 0.001	1.102	1.008-1.202	0.027
Left ventricle ejection fraction	0.895	0.875-0.916	< 0.001	0.954	0.898-0.976	< 0.001
Total ischemia time, min	1.006	1.005-1.007	< 0.001	1.007	1.005-1.009	< 0.001
Thrombus grade	4.311	2.594-7.163	< 0.001	2.317	1.284-4.179	0.005
Stent length, (per 1 mm)	1.064	1.047-1.081	< 0.001	1.054	1.032-1.091	< 0.001
Stent diameter, (per 1 mm)	2.678	1.695-4.230	< 0.001	2.128	1.186-4.354	0.011

by mortality, even in transient pacemaker-treated patients, has not yet been clearly demonstrated. Similar to our study, a study conducted by Auffret et al. established that HAVB is associated with reduced post pPCI TIMI flow[16]. However, in our study for the first time HAVB was found to be an independent predictor of no-reflow.

No-reflow is described as inadequate myocardial perfusion without evidence of vessel obstruction. The cause of no-reflow is complex and multifactorial. Despite not being completely elucidated, multiple mechanisms have been put forward as the cause of no-reflow, including tissue edema, distal embolization, spasm of microcirculation, platelet aggregation, neutrophilic plugging or a combination of these factors[17-19]. In STEMIs accompanied by HAVB, emergence of bradicardia and hypotension could decrease the cardiac output and perfusion pressure and increase possibility of intracoronary stasis. Therefore HAVB may make more prominent the mechanisms responsible for the etiopathogenesis of no-reflow. More importantly, right ventricular (RV) apical pacing may not give the desired result in terms of hemodynamics. It has been previously established that RV apical pacing and dysynchronicity, even in acute phase, change the electrical and mechanical activation pattern of the ventricles, which results in changes in cardiac metabolism and perfusion, oxygen demand, hemodynamics, and mechanical function[20]. The increase in oxygen demand and the reduction in perfusion capacity may accelerate or embody the development of no-reflow.

Limitations

The present study has several limitations. First, although the data were acquired prospectively, the study had a retrospective design and was based on a registry analysis and the number of patients with HAVB was low. Second, reperfusion success was evaluated only by visual assessment and a more specific and sensitive method, such as coronary flow reserve, contrast echocardiography or cardiac magnetic resonance, was not used. Finally, in this study, there is no information of permanent

pacemaker implantation records during in-hospital and long-term follow-up. Namely, this study does not answer whether patients with HAVB in the setting of STEMI will need permanent pacemakers in the long-term.

CONCLUSION

This study showed that HAVB the setting of STEMI is associated with long-term mortality in addition to short-term mortality. In this study, which was the first study to examine the impact of HAVB on reperfusion success, we have shown that HAVB is significantly related to no-reflow and is an independent predictor of no-reflow. Furthermore, patients who had no-reflow had a worse prognosis both in short- and long-term follow-up. In conclusion, HAVB should be closely monitored because of its association with no-reflow, and also because of the relationship between HAVB and mortality.

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CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: MÇ, YK

Analysis/Interpretation: MÇ, YK

Data Acquisition: MÇ, YK

Writting: MÇ, YK

Critical Revision: MÇ, YK

Final Approval: MÇ, YK

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