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Impact of Diabetes Mellitus on Myocardial Perfusion in Patients with ST-Segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention Using Distal Protection Devices

Chikara MORI, Kenichi HONGO, Nobutaka SATO, Joshi TSUTSUMI, Takahiro SHIBATA, and Michihiro YOSHIMURA

Division of Cardiology, Department of Internal Medicine, The Jikei University School of Medicine

ABSTRACT

Objective : The presence of diabetes mellitus (DM) is highly related to increased mortality in patients with ST-segment elevation myocardial infarction (STEMI) ; however, the mechanism(s) underlying the poor prognosis in patients with diabetes is not fully understood. In addition, although it has been reported that myocardial perfusion following primary percutaneous coronary intervention (PCI) is worse in patients with diabetes, the possible contribution of distal embolization in patients with diabetes is unclear. In the present study, we hypothesized that myocardial perfusion following primary PCI using a distal protection device would be different between patients with and without diabetes. Therefore, we evaluated the effect of DM on myocardial perfusion after primary PCI using distal protection devices, as assessed using myocardial blush grade (MBG) and ST-segment elevation resolution (STR) as clinical markers.

Methods : Thirty-one patients with diabetes and 51 patients without diabetes, and having STEMI treated with primary PCI using distal protection devices within 24 hours (h) from the onset of symptoms were examined. The MBG, STR, peak creatine kinase (CK) level, and left ventricular ejection fraction (LVEF) were compared between groups with and without DM.

Results : There was no significant difference in the post-procedural Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 between the group with diabetes and that without (100% vs. 100%, $P=1.0$). However, the DM group had a significantly lower incidence of complete STR and MBG 3 than the non-DM group (complete STR : 19% vs. 56%, $P<0.001$; MBG 3 : 41% vs. 82%, $P<0.001$). The LVEF and peak CK levels were similar in the two groups (LVEF 62% vs. 66%, $P=0.52$; peak CK levels 3124 vs. 3229, $P=0.86$).

Conclusions : There was no significant difference in the success rate for reperfusion, infarct size, or TIMI flow grade after primary PCI between patients with and without diabetes. However, microvascular perfusion was impaired in patients with diabetes, as estimated using STR and MBG. Compared to patients without diabetes, patients with diabetes had worse myocardial perfusion following primary PCI, even when a distal protection device combined with thrombus aspiration was used. (Jikeikai Med J 2015 ; 62 : 21-32)

Key words : acute myocardial infarction, diabetes mellitus, reperfusion injury, distal embolization, distal protection device

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森　　力，本郷　賢一，佐藤　伸孝，堤　　穣志，芝田　貴裕，吉村　道博

Mailing address : Chikara MORI, Division of Cardiology, Department of Internal Medicine, The Jikei University Daisan Hospital, 4-11-1 Izumihon-cho, Komae-shi, Tokyo 201-8601, Japan.

E-mail : c.mori@jikei.ac.jp

INTRODUCTION

Primary percutaneous coronary intervention (PCI) with stent implantation is the standard treatment for patients with ST-elevation myocardial infarction (STEMI)[1]. Primary PCI is known to result in better coronary reperfusion than thrombolytic therapy. Therefore, primary PCI is recognized to have better outcomes for STEMI patients[2,3].

Diabetes mellitus (DM) is an independent factor associated with acute and chronic prognoses in STEMI patients. Patients with DM have an increased mortality rate regardless of the use of reperfusion therapy (thrombolysis or primary PCI)[4]. DM leads to abnormal myocardial perfusion due to reduction in the coronary flow reserve[5] ischemic preconditioning, and coronary endothelial function[6,7]. Previous studies have suggested that acute outcomes of patients with diabetes having STEMI treated with primary PCI were superior to those of patients treated with thrombolytic therapy[8,9]. In addition, myocardial perfusion following reperfusion therapy in STEMI was worse in patients with diabetes than those without, as estimated using ST-segment elevation resolution (STR)[10] and myocardial blush grade (MBG)[11-13]. However, these previous studies used thrombolytic therapy or primary PCI alone and did not use distal protection devices[11,12]. Distal embolization of atheromatous and thrombotic materials is common after primary PCI. The prevention of distal embolization enhances myocardial perfusion and reduces infarct size and should improve the event-free survival after primary PCI, as supported by observational studies[14]. Distal embolization could be associated with higher mortality in patients with diabetes having STEMI treated with PCI[15].

We hypothesized that patients with diabetes would have worse myocardial perfusion following primary PCI even when a distal protection device combined with thrombus aspiration is used, as compared to patients without diabetes. Therefore, in the present study, we evaluated myocardial perfusion following primary PCI combined with distal protection devices for STEMI, in patients with or without DM, as assessed using STR and MBG, which are clinical markers of reperfusion.

METHODS

Study Population

A total of 82 patients with acute myocardial infarction (AMI) admitted to Fuji City General Hospital from January 2006 to March 2007 were studied. STEMI was defined as symptoms of ischemia with electrocardiographic (ECG) signs compatible with AMI (ST-elevation at the J point in two contiguous leads with cutoffs : ≥0.1 mV in all leads other than leads V2-3 where the following cut points apply : ≥0.2 mV in men ≥40 years ; ≥0.25 mV in men <40 years, or ≥0.15 mV in women), and detection of a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile of the upper reference limit[16]. Patients with cardiogenic shock and/or left main coronary artery stenosis >50% in diameter were excluded from the present study. Hypertension was defined as a history of systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or antihypertensive therapy. Dyslipidemia was defined as a fasting low-density lipoprotein cholesterol level ≥140 mg/dL, a fasting high-density lipoprotein cholesterol level <40 mg/dL, a fasting triglycerides level ≥150 mg/dL, or the need for antilipidemial therapy. In the present study, patients were considered to have DM if their medical records revealed a history of diabetes and they were being treated with a drug (insulin or oral hypoglycemic agents) or diet, or if they had fasting hyperglycemia (plasma glucose level >126 mg/dL) and glycated hemoglobin (HbA1c ; National Glycohemoglobin Standardization Program [NGSP])>6.5%[17]. We transformed the HbA1c (Japan Diabetes Society, JDS) levels to the HbA1c (NGSP) levels using the following formula : NSGP (%)=1.02×JDS (%)+0.25%. Plasma glucose was the non-fasting glucose level measured at the time of admission. Recent studies used 10.0 mmol/L or 11.0 mmol/L (1 mmol/L=18 mg/dL) of blood glucose levels on admission to define admission hyperglycemia[18]. Therefore, admission hyperglycemia was defined as an admission plasma glucose level >200 mg/dL (>11.1 mmol/L) regardless of the diabetes status in the present study. Of the 82 patients enrolled in the study, 31 were diagnosed as having DM. Informed consent was obtained from every patient before the procedures. This study conformed to the ethics guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committees of our institution (authorization number

25-334 7469) and Fuji City General Hospital (authorization number 87).

PCI Procedures

Acute coronary angiography was performed, followed by PCI to restore blood flow to a Thrombolysis In Myocardial Infarction (TIMI) flow grade of 3 in the infarct-related artery[19] by using a bare metal stent (BMS) within 24 h from the onset of continuous chest symptoms and typical ECG changes in STEMI. We excluded stable and asymptomatic patients who were treated more than 12 h after the onset of STEMI. All patients received 100 mg of aspirin and heparin (5,000 IU) intravenously, as well as nitroglycerin (1 mg) as an intracoronary injection before PCI, and were treated with a distal embolization protection device (GuardWire® Plus system, Medtronic Corp., Minneapolis, Minnesota USA) and examined by intravascular ultrasound. The GuardWire® Plus system consists of a guidewire incorporating a central inflation lumen distally attached to an elastomeric balloon. In brief, the guidewire was introduced into the infarct-related artery, and aspiration of any thrombus was performed. Then, an elastomeric balloon was placed and inflated distal to the culprit lesion to protect against any distal embolization. A BMS was implanted either immediately or before dilatation with a small balloon, depending on the characteristics of the lesion. After stent implantation, angiographic optimization was performed by balloon dilatation appropriately under distal protection using the GuardWire® Plus system. Stent implantation was performed within 1 h of arrival at the hospital in all patients. Procedural success was defined as residual stenosis <25% without major complications (i.e., death, repeat PCI or the need for emergency coronary artery bypass surgery). Following PCI, left ventriculography (LVG) was performed. All patients were treated with dual anti-platelet therapy (aspirin, 100 mg daily and ticlopidine 200 mg twice daily) for at least four weeks after the procedure. Six months after the procedure, we performed follow-up coronary angiography and an LVG study.

ECG Analysis

A 12-lead ECG was recorded immediately before and immediately after the procedure. The analyses were performed by one observer unaware of the angiographic and clinical data. The sum of the ST-segment elevations were measured 20 ms after the end of the QRS complexes. The summed level of ST-segment elevations was calculated for an anterior myocardial infarction in V_1 to V_6, I, and aVL. This value for an inferior myocardial infarction was measured in leads II, III, aVF, V5, and V6. STR was calculated as the initial sum of the ST-segment elevations minus the sum of the ST-segment elevations on the second ECG, divided by the initial sum of the ST-segment elevations, and was expressed as a percentage value. STR was classified as complete (>70%), partial (30% to 70%), or absent (<30%)[10]. Figure 1 shows a representative example of STR.

Visual Assessment of Flow

The perfusion status of the coronary artery was determined in accordance with the TIMI study classification[19]. The myocardial blush was graded according to the dye density score proposed by van't Hof et al.[11] : MBG 0 to 1 indicated minimal-to-no myocardial blush or contrast density (relative to the dye density in uninvolved areas) ; MBG 2 was moderate myocardial blush and MBG 3 was normal blush. MBG was evaluated immediately after a PCI procedure. Figure 2 shows a representative example of MBG.

Assessment of the Infarct Size

The serum creatine kinase (CK) and creatine kinase MB (CK-MB) levels were measured on admission and every 3 h until the CK and CK-MB levels peaked, and those values were used as enzymatic markers of the infarct size. The LVEF was measured using the area-length method in LVG.

Statistical Analyses

Continuous data are expressed as mean±SD. The statistical analyses were performed using the chi-square test for categorical data and Student's *t*-test for continuous data. Multiple logistic regression analysis was performed to assess independent predictors of impaired reperfusion. Candidate predictors included admission glucose, admission hyperglycemia, HbA1c, age, gender, dyslipidemia, diabetes, hypertension, smoking history, and body mass index. We used the MedCalc statistical software, version 14.10.2 (MedCalc Software, Ostend, Belgium). A value of $P<0.05$ was considered statistically significant.

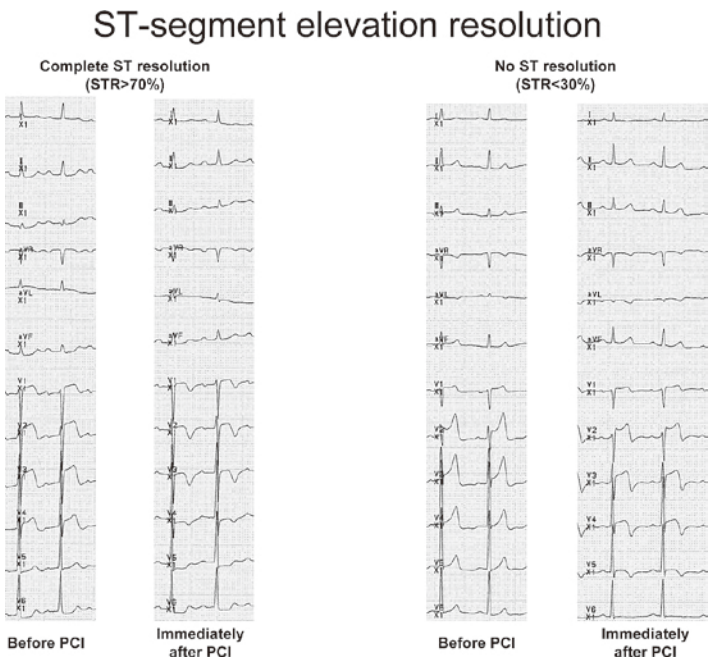

Fig. 1. ST-segment elevation resolution
The 2 panels on the left demonstrate a representative case of complete ST-segment elevation resolution. The summed level of ST-segment elevation (V1 to V6, I, and aVL) before PCI decreased >70% immediately after PCI. The 2 panels on the right demonstrate a representative case of the absence of ST-segment elevation resolution. The summed level of ST-segment elevation before PCI decreased by <30% immediately after PCI.
PCI, percutaneous coronary intervention

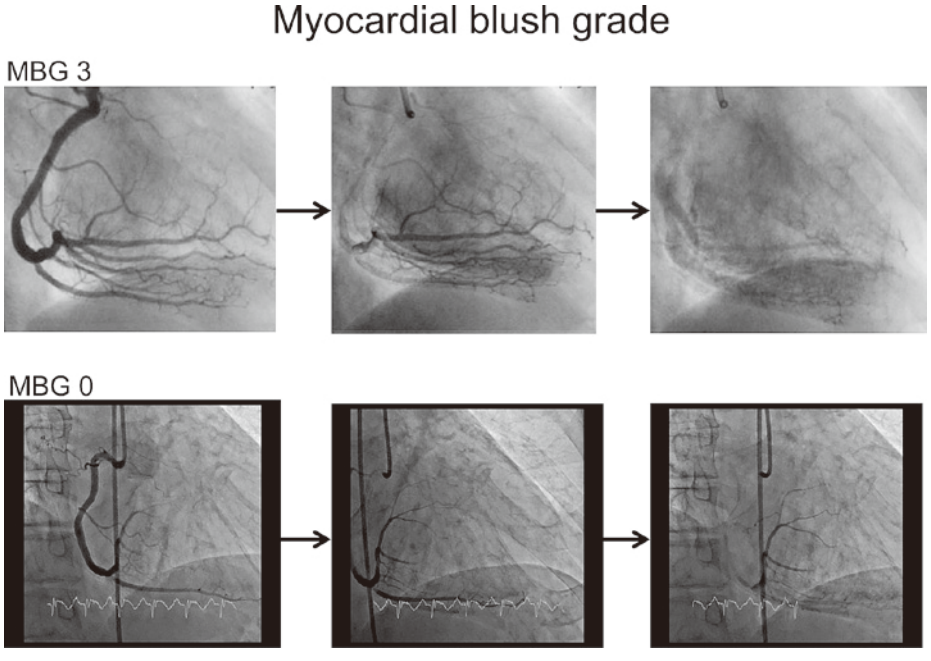

Fig. 2. Myocardial blush grade
The upper panel demonstrates a representative result of MBG 3. Following right coronary angiography (left), contrast medium deeply stained the myocardium (middle) and was then quickly washed out (right).
The lower panel demonstrates a representative result of MBG 0. Following coronary angiography (left), contrast medium did not stain the myocardium (middle and right).
MBG ; myocardial blush grade.

Results

Baseline Characteristics

The baseline characteristics of the patients are shown in Table 1. There were no significant differences in the baseline characteristics of the two groups, except for the glycemic profile. Although the incidence of dyslipidemia was lower in the non-DM group, the difference was not statistically significant. In terms of the glycemic profile, the plasma glucose and HbA1c levels on admission were significantly lower in the non-DM group than in the DM group. The number of patients with admission hyperglycemia was significantly smaller in the non-DM group than in the DM group.

Angiographic and Procedural Characteristics

All patients underwent coronary thrombectomy and BMS implantation. The epicardial coronary flow following primary PCI was TIMI grade 3 in all patients. Table 2 shows the angiographic and procedural characteristics of the two groups. TIMI flow grades before and after PCI, percent diameter stenosis, lesion length, stent size, and stent length were similar between the two groups.

ST- Segment Elevation Resolution (STR) and Myocardial Blush Grade (MBG)

Table 3 shows a comparison of STR and MBG between patients with and without diabetes. Complete STR occurred in six patients (19.3%) in the DM group and in 29 patients (56.8%) in the non-DM group ($P<0.001$). The incidences of partial STR in patients with and without diabetes were 12 (38.7%) and 15 (29.4%), respectively, while 13 patients (41.9%) in the DM group and seven (13.7%) in the non-DM group showed no STR ($P<0.01$).

MBG 3 was observed after primary PCI in 13 patients (41.9%) in the DM group and in 42 patients (82.3%) in the non-DM group ($P<0.001$). MBG 2 was present in nine patients (29.0%) in the DM group and four patients (7.8%) in the non-DM group ($P=0.01$). MBG 0 or 1 was present in nine patients (29.0%) in the DM group and five patients (9.8%) in the non-DM group ($P=0.02$).

We also analyzed data of STR and MBG in male and female patients independently (Table 4). Among male patients, complete STR occurred in 3 (13.3%) in the DM group and 21 (53.8%) in the non-DM group ($P<0.01$), and MBG 3 was observed in 9 patients (39.1%) in the DM group and in 32 patients (82.0%) in the non-DM group ($P<0.001$). Among female patients, complete STR occurred in 3 (37.5%) in the DM group and 8 (66.6%) in the non-DM group ($P=0.76$), and MBG 3 was observed in 4 patients (50%) in the DM group and in 11 patients (91.6%) in the non-DM group ($P=0.03$).

We then evaluated the role of admission hyperglycemia on myocardial reperfusion. Table 5 shows differences in STR and MBG between patients with hyperglycemia (admission plasma glucose level>200 mg/dL) and patients without hyperglycemia (admission plasma glucose <200 mg/dL). In the hyperglycemia group, complete STR was observed in a significantly fewer patients and the absence of STR was found at a significantly higher rate than that in

Table 1. Baseline characteristics of the patients

	Non-DM group ($n=51$)	DM group ($n=31$)	P value
Age (years)	65±10	63±12	0.46
Male, *n* (%)	39 (76)	23 (76)	0.81
BMI (kg/m^2)	23.7±3.5	24.0±3.8	0.61
Glycemic profile			
Admission plasma glucose (mg/dl)	147±34	249±142	<0.001
Patients with admission hyperglycemia *n* (%)	18 (35.2)	1 (3.2)	<0.001
HbA1c (%)	5.9±0.8	8.3±2.7	<0.0001
Coronary risk factors			
Hypertension, *n* (%)	36 (70)	20 (76)	0.56
Dyslipidemia, *n* (%)	28 (54)	23 (74)	0.08
Smoking, *n* (%)	26 (50)	16 (51)	0.95

BMI, body mass index ; HbA1c, hemoglobin A1c. Continuous data are expressed as mean±SD.

Table 2. Angiographical and procedural characteristics of the patients

	Non-DM group (n=51)	DM group (n=31)	P value
TIMI flow grade before PCI			
0	31 (60)	18 (58)	0.8
1	6 (11)	4 (12)	0.87
2	12 (23)	7 (22)	0.87
3	2 (4)	2 (6)	0.6
Culprit lesion			
LAD, n (%)	29 (56)	15 (48)	0.45
LCX, n (%)	2 (4)	2 (6)	0.6
RCA, n (%)	20 (39)	14 (45)	0.59
ACC/AHA lesion class type			
A, n (%)	1 (1)	0 (0)	0.42
B1, n (%)	13 (25)	14 (45)	0.06
B2, n (%)	30 (58)	12 (38)	0.07
C, n (%)	7 (13)	5 (16)	0.76
Percent diameter stenosis (%)	96±9.4	97±8.4	0.65
Post percent diameter stenosis (%)	4.2±5.6	4.4±5.7	0.83
Lesion length (mm)	14±5.6	16±8.7	0.33
Reference diameter (mm)	2.9±0.4	3.0±0.5	0.34
Stent size (mm)	3.6±0.3	3.6±0.3	0.64
Stent length (mm)	18±4.8	18±5.7	0.85
Stent numbers	1.0±0.1	1.0±0.1	0.87
Binary restenosis, n (%)	8 (15.6)	5 (16.4)	0.95
Angiographically driven TLR, n (%)	5 (9.8)	2 (6.4)	0.59

TIMI, Thrombolysis In Myocardial Infarction study classification ; LAD, left anterior descending artery ; LCX, left circumflex artery ; RCA, right coronary artery ; TLR, Target Lesion Revascularization. Continuous data are expressed as mean±SD.

Table 3. Comparison of the incidence of ST-segment elevation resolution (STR) and myocardial blush grade (MBG) between the non-DM and DM groups

	Non-DM group (n=51)	DM group (n=31)	P value
ST-segment elevation resolution			
Absent, n (%)	7 (13.7)	13 (41.9)	<0.01
Partial, n (%)	15 (29.4)	12 (38.7)	0.38
Complete, n (%)	29 (56.8)	6 (19.3)	<0.001
Myocardial blush grade			
0 or 1, n (%)	5 (9.8)	9 (29.0)	0.02
2, n (%)	4 (7.8)	9 (29.0)	0.01
3, n (%)	42 (82.3)	13 (41.9)	<0.001

the non-hyperglycemia group. MBG 3 was significantly lower in the hyperglycemia group ; however, MBG 0 or 1 was not significantly different from the non-hyperglycemia group.

We performed multivariable analysis and found that DM was an independent predictor of complete STR, while DM and admission hyperglycemia were independent predictors of MBG 3 (Table 6).

Biomarkers and Left Ventriculography data

The LVEF immediately after primary PCI in the DM group was similar to that the non-DM group (58%±2% vs.

Table 4. Comparison of gender-related incidence of ST-segment elevation resolution (STR) and myocardial blush grade (MBG) between the non-DM and DM groups

Male			
	Non-DM group (n=39)	DM group (n=23)	P value
ST-segment elevation resolution			
Absent, n (%)	6 (15.3)	12 (13.3)	<0.01
Partial, n (%)	12 (30.7)	8 (34.7)	0.74
Complete, n (%)	21 (53.8)	3 (13.3)	<0.01
Myocardial blush grade			
0 or 1, n (%)	6 (15.3)	4 (17.3)	0.83
2, n (%)	1 (2.5)	10 (43.4)	<0.001
3, n (%)	32 (82.0)	9 (39.1)	<0.001
Female			
	Non-DM group (n=12)	DM group (n=8)	P value
ST-segment elevation resolution			
Absent, n (%)	1 (8.3)	1 (12.5)	0.19
Partial, n (%)	3 (25.0)	4 (50.0)	0.25
Complete, n (%)	8 (66.6)	3 (37.5)	0.76
Myocardial blush grade			
0 or 1, n (%)	0 (0)	2 (25.0)	0.06
2, n (%)	1 (8.3)	2 (25.0)	0.30
3, n (%)	11 (91.6)	4 (50.0)	0.03

Table 5. Comparison of the incidence of ST-segment elevation resolution (STR), myocardial blush grade (MBG), and glycemic profile between patients with and without admission hyperglycemia

	Admission Hyperglycemia (−) (n=63)	Admission hyperglycemia (+) (n=19)	P value
ST-segment elevation resolution			
Absent, n (%)	10 (15.8)	9 (47.3)	<0.01
Partial, n (%)	21 (33.3)	7 (36.8)	0.77
Complete, n (%)	32 (50.7)	3 (16.6)	<0.01
Myocardial blush grade			
0 or 1, n (%)	9 (14.2)	3 (15.7)	0.95
2, n (%)	7 (11.1)	7 (36.8)	<0.01
3, n (%)	47 (74.6)	9 (47.3)	0.02
Glycemic profile			
Admission plasma glucose (mg/dl)	144.8±28.6	316.6±135.1	<0.0001
HbA1c (%)	5.7±0.3	8.9±3.0	<0.0001

Continuous data are expressed as mean±SD.

62%±1%, P=0.52). The maximum mean serum CK and CK-MB levels after PCI in the DM group were also similar to those in the non-DM group (CK levels : 3.229±489 vs. 3.124±358, P=0.86 ; CK-MB levels : 281±34 vs. 298±36, P=0.73). At 6 months after PCI, the LVEF was not significantly different between the DM and non-DM groups (59% ±2% vs. 61%±2%, P=0.90).

Restenosis Rate and Target Lesion Revascularization

Restenosis rate at 6 months after PCI was not signifi-

Table 6. Multivariate predictors of complete ST-segment elevation resolution (STR) and myocardial blush grade (MBG) 3

Complete ST segment resolution			
Variable	Odds ratio	95% CI	*P* value
Diabetes mellitus	0.12	0.03–0.49	<0.01
Dyslipidemia	0.82	0.25–2.67	0.74
Admission glucose	0.99	0.98–1.00	0.59
Admission hyperglycemia	1.68	0.23–11.8	0.60
HbA1c	0.96	0.65–1.42	0.86
Gender	0.39	0.08–1.76	0.22
Age	0.97	0.91–1.02	0.28
Myocardial brush grade 3			
Variable	Odds ratio	95% CI	*P* value
Diabetes mellitus	0.16	0.03–0.76	0.02
Dyslipidemia	1.71	0.55–5.34	0.34
Admission glucose	1.01	0.99–1.03	0.08
Admission hyperglycemia	0.03	0.00–0.69	0.02
HbA1c	0.97	0.53–1.76	0.92
Gender	1.07	0.26–4.29	0.91
Age	1.05	0.99–1.11	0.91

CI, confidence interval

cantly different between the DM and non-DM groups (P=0.95). Target lesion revascularization (TLR) was also found to be similar in both groups (P=0.59 ; Table 2).

Discussion

The present study revealed that patients with diabetes have worse myocardial perfusion following primary PCI than those without, even when a distal protection device combined with thrombus aspiration is used. The epicardial coronary flow following primary PCI combined with a distal protection device was TIMI grade 3 in all STEMI patients. However, the myocardial reperfusion estimated using STR and MBG was significantly disturbed in patients with diabetes, irrespective of the baseline TIMI flow or infarct artery distribution. To the best of our knowledge, the present study is the first to investigate the correlation between myocardial perfusion following primary PCI using a distal protection device in all patients and specifically in those with diabetes.

Previous studies have reported that myocardial reperfusion was worse in patients with diabetes than in those without. A substudy from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial revealed that a significantly higher number of patients with diabetes than those without have a final MBG 0/1 (56% vs. 47%, P=0.014), although the final TIMI grade 3 flow rates were similar between patients with diabetes and those without[12]. In addition, the Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberated Debris (EMERALD) trial also reported that was significantly higher number of patients with diabetes (34%) had a final MBG of 0/1 than patients without diabetes (16%) (P=0.002)[13]. Compared with these two studies, our study population revealed a smaller number of patients who had final MBG of 0/1 (29% in the diabetic group and 4% in the non-diabetic group). This discrepancy might be because a substudy from the CADILLAC trial used stents for only 50% of all patients, while a substudy from the EMERALD trial used distal protection devices for only 31% of DM and 53% of non-DM cases. Because we used stent implantation and distal protection devices in all of our patients, the number of patients with final MBG of 0/1 reduced in the present study. In particular, the number of patients with a final MBG of 0/1 was much lower in the non-DM population in the present study than those in the CADILLACl[12] and

EMERALD trials[13]. This result suggests that the combination of thrombus aspiration and distal protection could improve myocardial reperfusion after PCI in STEMI, even in the non-DM population.

Distal embolization can occur during reperfusion therapy for AMI due to a thrombus or plaque debris, and can lead to mechanical capillary obstruction of the coronary artery[20]. Distal embolization also produces endothelial dysfunction and local inflammation, which worsens myocardial reperfusion[21]. Mechanical devices, such as distal protection devices or thrombus aspiration devices, reduce distal embolization during primary PCI and increase the success rate of PCI[22,23]. TIMI myocardial perfusion grade and MBG after PCI in AMI patients could be improved using distal protection devices alone or combination with intracoronary thrombectomy[24]. Therefore, these devices can be effective in initially restoring coronary blood flow after PCI in patients with AMI.

Although the mechanism(s) responsible for a worse microvascular injury in patients with diabetes remains to be fully elucidated, there have been several reports regarding possible reasons for this finding. For example, microvascular spasm can occur owing to a dysfunction of the coronary endothelial and smooth muscle cells, which is induced by a disturbance of nitric oxide bioavailability and increased oxidative stress[25]. Diabetes promotes prothrombotic and antifibrinolytic abnormalities and an inflammatory state, leading to leukocyte accumulation and microthrombus formation in the coronary microcirculation[25,26]. The acute recruitment of collateral function after recanalization is also impaired in patients with diabetes[27].

The role of the plasma glucose level at admission on mortality and prognosis after AMI has been receiving attention[28]. Experimental and clinical studies have reported the possible mechanism underlying poor outcomes resulting from hyperglycemia at admission in AMI patients. Admission hyperglycemia was reported to induce endothelial apoptosis and endothelial dysfunction[29,30], to activate platelet aggregation and coagulation[31,32], and to increase oxidative stress and the production of excessive inflammation[33]. In the present study, the admission plasma glucose level in DM group was significantly higher than that in the non-DM group, and the number of patients with admission hyperglycemia was also significantly higher in the DM group than in the non-DM group. Myocardial perfusion estimated using STR and MBG was significantly worse in the admission hyperglycemia group compared with the non-admission hyperglycemia group. In addition, admission hyperglycemia was an independent predictor of MBG 3. Therefore, it is possible that admission hyperglycemia is also related to reduced myocardial reperfusion in patients with diabetes even after distal embolization is reduced.

The impact of gender on the rate of mortality in acute coronary syndrome is controversial. Berger et al.[34] suggested that female patients had a higher mortality rate in the setting of STEMI. However, the differences in mortality rates between patients with and without diabetes were independent of gender. In the present study, myocardial perfusion after PCI was different between male and female patients. In particular, complete STR was worse only in male patients with DM. Because manifestation of coronary artery disease can be affected by various risk factors, it is necessary to investigate the role of DM and gender difference on myocardial perfusion in appropriate conditions.

In the present study, LVEF at 6 months after AMI was not significantly different between patients with and without diabetes. A previous report showed an association between impaired myocardial perfusion after PCI, a larger infarction and a poorer prognosis in patients with diabetes having AMI[13]. However, this study used distal protection devices less frequently, especially in the DM population, and not all of the patients achieved a final TIMI 3 flow (90%). Because our study provided a final TIMI 3 flow in all the patients, the left ventricular function would be more likely to be preserved 6 months after AMI, even in patients with diabetes. Previous reports also demonstrated the prognostic impact of the peak CK levels and reduced LVEF on the clinical outcomes in patients with AMI[35,36]. Therefore, the absence of any differences in LVEF may have been due to the lack of differences in the peak CK levels between the two populations. In addition, LVEF at 6 months after AMI was not significantly different from the value at baseline in both patients with and without diabetes. This might also be due to good reperfusion (TIMI 3 flow in all the patients) and a low level of peak CK value.

Although restenosis rate and TLR at 6 months after PCI was almost the same in patients with and without diabetes, we do not have enough data on the long-term prognosis, including mortality, in the present study. However, it has been reported that the mortality rate was high in pa-

tients with diabetes because of diminished microvascular perfusion[12]. Therefore, disturbance in microvascular reperfusion in our patients with diabetes may have adversely affected long-term outcomes.

LIMITATIONS

The present study has several potential limitations. First, this study used data from patients enrolled about 7 years ago. Therefore, there are some discrepancies between our management for the treatment of STEMI then and our current management. We used BMS in all of the patients in the present study. Recently, second generation drug-eluting stents (DES) are frequently used for PCI in ACS. It has been reported that TIMI grade 3 after the procedure was not statistically different between patients receiving DES and BMS for STEMI[37]. Because structures of the stent platform are the same between DES and BMS, reperfusion injury just after reperfusion therapy in AMI should not be different. To the best of our knowledge, there has not been a previous report comparing STR or MBG following PCI for STEMI in groups receiving DES and BMS. Although the long-term angiographic outcome was superior in DES, myocardial reperfusion after PCI might not be very different between DES and BMS. Use of ticlopidine instead of the newer P2Y12 inhibitors (e.g., clopidogrel or prasugrel) is another different factor from the current era. In the present study, we used ticlopidine for only 4 weeks after BMS implantation. The use of P2Y12 inhibitors would likely not affect our results. Second, some patients included in the non-DM group may have had diabetes, but not had a diagnosis of diabetes, because we did not perform routine oral glucose tolerance testing to diagnose DM in non-diabetic group. Third, this study was a non-randomized, single-center observational study performed on a relatively small sample size. Fourth, we do not have enough information regarding the long-term prognosis after AMI to analyze the impact on long-term outcome. Therefore, it will be necessary to evaluate long-term prognosis, and to include a larger number of subjects to confirm the present results. Fifth, one observer unaware of the angiographic and clinical data assessed the ST resolution visually to minimize the potential for bias in the present study. This might have uncertainty in the reproducibility of this measurement.

CONCLUSION

Myocardial reperfusion was significantly disturbed in DM patients with STEMI undergoing PCI using distal protection devices, irrespective of the baseline TIMI flow or infarct artery distribution. Our results suggest that the decreased myocardial reperfusion in patients with diabetes may be due to factors other than mechanical capillary obstruction. A future study with an increased number of patients is warranted to confirm these findings.

Authors have no conflict of interest.

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