



Comparison of clinical outcomes between sufficient versus insufficient diagonal branch flow in anterior acute myocardial infarction

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Abstract

In primary percutaneous coronary intervention (PCI), revascularization to the main branch is considered to be more important than that to the side branch. The purpose of the present study was to compare in-hospital clinical outcomes between sufficient and insufficient diagonal flow in patients with anterior ST-elevation acute myocardial infarction. A total of 229 left anterior descending artery (LAD)-AMI with final Thrombolysis in Myocardial Infarction (TIMI)-3 LAD flow were included, and divided into the sufficient diagonal flow group (TIMI-3 diagonal flow: $n = 170$) and the insufficient diagonal flow group (TIMI ≤ 2 diagonal flow: $n = 59$). The primary endpoint was the incidence of mechanical complication. The secondary endpoints were incidences of in-hospital death, heart failure at discharge, and left ventricular thrombus. There were no significant differences in the primary endpoint (the sufficient diagonal flow group: 1.2%, the insufficient diagonal flow group: 0%, $P = 0.403$). In-hospital death was more frequently observed in the insufficient diagonal flow group (8.5%) than the sufficient diagonal flow group (2.9%) without reaching statistical significance ($P = 0.073$). The incidence of heart failure at discharge, and thrombus in left ventricular were not different between the two groups. In conclusion, in-hospital outcomes were not significantly different between the sufficient and insufficient diagonal flow groups. We may not stick to the diagonal flow in LAD-STEMI, as long as the LAD flow is maintained by PCI.

Keywords Acute myocardial infarction · Left anterior descending artery · Diagonal branch · Percutaneous coronary intervention

Introduction

The primary percutaneous coronary intervention (PCI) is the cornerstone for ST-elevation acute myocardial infarction (STEMI) [1, 2]. The goal of the primary PCI is to obtain Thrombolysis In Myocardial Infarction (TIMI)-3 flow as soon as possible, because final TIMI flow and doortoballoon time are closely associated with clinical outcomes in acute myocardial infarction (AMI) patients [3, 4]. Therefore, simple and speedy procedures are preferred in the primary PCI. Revascularization to the main branch is considered to be more important for clinical outcomes in STEMI patients than that to the side branch, because the procedure of side

branch treatment including kissing balloon technique (KBT) requires more contrast media and procedure time that are associated with more risk of stent thrombosis during procedure [5, 6].

On the other hand, the incidence of left ventricular free wall rupture was higher in the side branch-AMI than in the main branch-AMI [7], suggesting the necessity of primary PCI to the branch lesion when the branch lesion is the culprit of AMI. However, it has not been discussed when the culprit lesion of AMI is the main branch involving side branches. For example, when the culprit of STEMI is the proximal segment or middle segment of the left anterior descending artery (LAD), diagonal branches as well as the LAD should be obstructed or severely narrowed. It is unknown that the combination of TIMI-3 flow in the LAD (main vessel) and TIMI ≤ 2 flow in the diagonal branch (side branch) would increase mechanical complications such as left ventricular free wall rupture.

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We hypothesized that the combination of TIMI-3 flow in the LAD and $\text{TIMI} \leq 2$ flow in the diagonal branch would not increase the incidence of in-hospital adverse events such as mechanical complications. The purpose of the present study was to compare in-hospital clinical outcomes between sufficient (TIMI-3) and insufficient ($\text{TIMI} \leq 2$) diagonal flow in patients with anterior STEMI with TIMI-3 LAD flow.

Methods

Study design

The present study was a retrospective and single-center study. We included STEMI patients whose culprit was the LAD between January 2014 and March 2017. We excluded patients whose final TIMI flow grade of LAD was ≤ 2 . The study population was divided into patients whose final TIMI flow grade of the diagonal branches was 3 (the sufficient diagonal flow group) and patients whose final TIMI flow grade of the diagonal branches were ≤ 2 (the insufficient diagonal flow group). If the number of diagonal branches were ≥ 3 , the largest branch and the second largest branch were adopted as the diagonal branch. The sufficient diagonal flow group required TIMI-3 flow of all diagonal branches, whereas the impaired diagonal flow group required at least one $\text{TIMI} \leq 2$ flow of diagonal branches. The difference between the two groups is described in Fig. 1. We excluded patients that underwent coronary artery bypass grafting for AMI. We also excluded patients who did not undergo any angioplasty, had in-stent occlusion, or had in-stent restenosis including stent thrombosis.

The primary endpoint was the incidence of mechanical complications during hospitalization. The secondary

endpoints were incidences of in-hospital death, heart failure at discharge, left ventricular thrombus, left ventricular wall motion score index (LVWMSI) in echocardiography during admission mechanical complications included cardiac rupture, ventricular septal perforation, and acute mitral regurgitation due to papillary muscle rupture. Heart failure was defined as the clinical condition that had volume overload and required diuretics at discharge [8, 9]. Left ventricular was evaluated in the echocardiography to divide left ventricular 17 sections and score motion of each sections [10]. The scores of 1, 2, 3, and 4 are given to normal or hyperkinetic, hypokinetic, akinetic, and dyskinetic or aneurysmal segments, respectively. The LVWMSI was calculated as the mean score of total visualized scores [11].

Clinical outcomes were acquired from hospital records. This study was approved by the institutional review board and written informed consent was waived, because of the retrospective study design.

Definitions

In the present study, AMI was defined as persistent chest pain, elevation of cardiac enzyme (at least twofold increases from normal upper limit) and ST-segment elevation or depression in electrocardiograms [12]. Diagnostic ST elevation was defined as new ST elevation at the J point in at least 2 contiguous leads of 2 mm (0.2 mV) and others were defined as non-ST elevation [13, 14]. Hypertension was defined as systolic blood pressure > 140 mmHg, diastolic blood pressure > 90 mmHg, or medical treatment for hypertension. Diabetes mellitus was defined as a hemoglobin A1c level $> 6.5\%$ or treatment for diabetes mellitus. Hyperlipidemia was defined as a total cholesterol level > 220 mg/dl, a low-density lipoprotein cholesterol level > 140 mg/dl, or treatment for hyperlipidemia [15]. Chronic kidney disease was defined as estimate glomerular filtration rate (eGFR) < 60 ml/min [13].

Percutaneous coronary interventions

Primary PCI was performed using standard techniques via radial artery, femoral artery or rarely brachial artery [15, 16]. First, we advanced a conventional guidewire across the lesion, and used a small balloon or thrombus aspiration catheter. The choice of devices including type of stent was left to the discretion of each interventional cardiologist. Activated coagulation time (ACT) was maintained > 250 s during PCI.

Statistical analysis

Data were expressed as mean \pm SD or percentage. Categorical variables were presented as numbers (percentage) and were compared using the Chi-square test (or Fisher exact

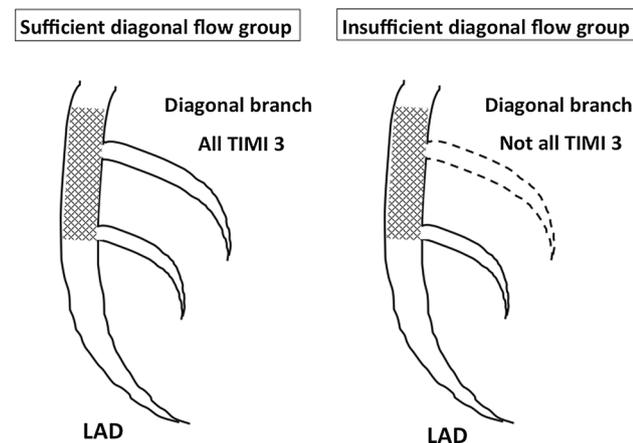


Fig. 1 The schema that illustrates the difference between the sufficient diagonal flow and insufficient diagonal flow groups

test for small samples). Continuous variables were compared using student's *t* test. Multivariate logistic regression analysis was applied to investigate the association between the insufficient diagonal flow group and in-hospital death after controlling confounding factors ($P < 0.05$ between the two groups). Statistical significance was defined as a two-sided value of $P < 0.05$. Statistical analyses were performed using SPSS 18.0/Windows (Chicago, Illinois, USA).

Results

Between January 2014 and December 2017, 295 patients were LAD-STEMI. A final study population consisted of the sufficient diagonal flow group ($n = 170$) and the insufficient diagonal flow group ($n = 59$) (Fig. 2).

The comparison of baseline clinical characteristics is shown in Table 1. Mean age was similar between the two groups. The frequency of IABP support was significantly higher in the insufficient diagonal flow group (23.7%) than in the sufficient diagonal flow group (7.6%) ($P = 0.001$). Ejection fraction of the insufficient diagonal flow group was significantly less in the impaired diagonal flow group

($46.6 \pm 13.7\%$) than in the sufficient diagonal flow group ($53.3 \pm 13.7\%$) ($P = 0.007$).

The comparison of lesion and procedural characteristics is shown in Table 2. Initial LAD TIMI flow was significantly lower in the insufficient diagonal flow group (0.8 ± 1.0) than the sufficient diagonal flow group (1.3 ± 1.2) ($P = 0.006$). Similarly, initial diagonal TIMI flow was significantly lower in the insufficient diagonal flow group (1.1 ± 1.2) than the sufficient diagonal flow group (2.0 ± 1.3) (1.05 ± 1.16 in the impaired diagonal flow group and 1.96 ± 1.28 in the sufficient diagonal flow group, $P < 0.001$). The frequency of femoral approach was significantly higher in the impaired diagonal flow group (45.8%) than in the sufficient diagonal flow group (30.0%) ($P = 0.028$).

The comparison of in-hospital outcomes is shown in Table 3. Mechanical complications were rarely observed in the sufficient diagonal flow group (1.2%), whereas there were no mechanical complications in the insufficient diagonal flow group (0%) ($P = 0.403$). The frequency of in-hospital death tended to be higher in the insufficient diagonal flow group (8.5%) than the sufficient diagonal flow group (2.9%) ($P = 0.073$). There were no significant differences in heart failure at discharge (the sufficient diagonal flow

Fig. 2 The study flow chart. *NSTEMI* nonST elevated myocardial infarction, *STEMI* ST elevated myocardial infarction, *LAD* left anterior descending artery, *MV* main vessel, *CABG* coronary artery bypass grafting

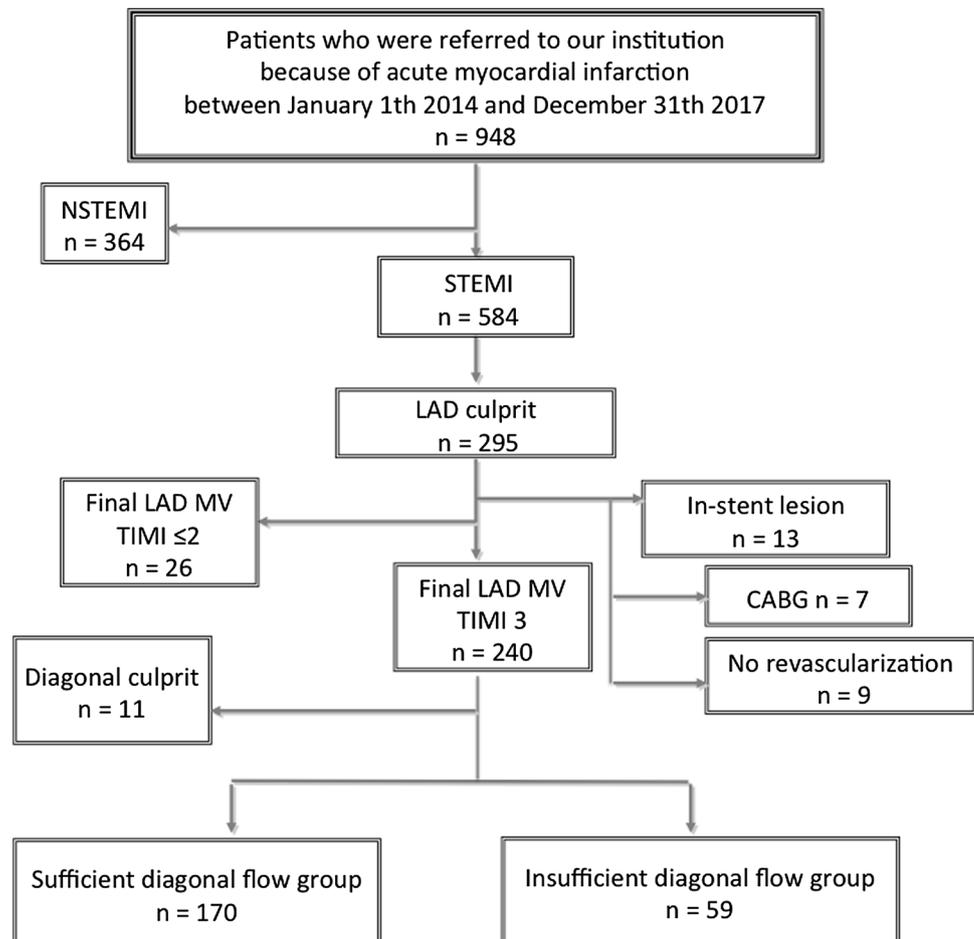


Table 1 Clinical characteristics between the sufficient and impaired diagonal flow groups

Variables	Sufficient diagonal flow (<i>n</i> =170)	Impaired diagonal flow (<i>n</i> =59)	<i>P</i> value
Patient characteristics			
Age (years)	69 ± 15	69 ± 19	0.795
Men, no. (%)	131 (77.1)	45 (76.2)	0.902
Hypertension, no. (%)	146 (85.9)	49 (83.1)	0.593
Diabetes mellitus, no. (%)	58 (34.1)	28 (47.5)	0.068
Hyperlipidemia, no. (%)	92 (54.1)	31 (52.5)	0.834
Chronic kidney disease, no. (%)	44 (25.9)	21 (35.6)	0.154
Hemodialysis, no. (%)	5 (2.9)	6 (10.2)	0.025
Current smoking, no. (%)	50 (29.4)	22 (37.3)	0.262
Previous myocardial infarction, no. (%)	4 (2.4)	4 (6.8)	0.111
Previous percutaneous coronary intervention, no. (%)	7 (4.1)	4 (6.8)	0.410
Previous coronary artery bypass grafting, no. (%)	1 (0.6)	2 (3.4)	0.103
Shock, no. (%)	11 (6.5)	7 (11.9)	0.185
Cardio-pulmonary arrest, no. (%)	11 (6.5)	4 (6.8)	0.934
Ventricular tachycardia/ventricular fibrillation, no. (%)	14 (8.2)	2 (3.4)	0.208
Systolic blood pressure at admission (mmHg)	142.6 ± 34.7	134.8 ± 39.0	0.098
Diastolic blood pressure at admission (mmHg)	84.6 ± 22.5	80.4 ± 23.1	0.158
Catecholamine use, no. (%)	13 (7.6)	7 (11.9)	0.323
IABP support, no. (%)	13 (7.6)	14 (23.7)	0.001
PCPS support, no. (%)	4 (2.4)	4 (6.8)	0.111
Peak CK (IU/L)	2240 ± 2520	3041 ± 3667	0.434
Peak CK-MB (IU/L)	204 ± 253	310 ± 364	0.141
Medication at admission			
Aspirin, no. (%)	19 (11.2)	12 (20.3)	0.076
Thienopyridine, no. (%)	9 (5.3)	4 (6.8)	0.671
Statin, no. (%)	30 (17.6)	9 (15.3)	0.674
ACE-inhibitor/ARB, no. (%)	57 (33.5)	18 (45.8)	0.670
Beta-blocker, no. (%)	15 (8.8)	9 (15.3)	0.165
Calcium channel blocker, no. (%)	54 (31.8)	14 (23.7)	0.244
Loop diuretics, no. (%)	15 (8.8)	6 (10.1)	0.758
Oral hypoglycemic agent, no. (%)	30 (17.6)	14 (23.7)	0.307
Insulin, no. (%)	5 (5.9)	4 (6.8)	0.191
Ejection fraction (%)	53.3 ± 13.7	46.6 ± 13.7	0.007

Data are expressed as the mean ± SD or number (percentage). A Student's *t* test was used for normally distributed continuous variables, a Mann–Whitney *U* test was used for abnormally distributed continuous variables, and a Chi-square test was used for categorical variables

STEMI ST elevated myocardial infarction, *NSTEMI* ST elevated myocardial infarction, *IABP* intra-aortic balloon pumping, *PCPS* percutaneous cardio-pulmonary support, *ACE* angiotensin converting enzyme, *ARB* angiotensin II receptor blocker

group: 32.9%, the insufficient diagonal flow group: 42.4%, $P=0.192$), and thrombus in left ventricular (the sufficient diagonal flow group: 2.4%, the insufficient diagonal flow group: 6.8%, $P=0.117$). The LVWMSI was significantly lower in the sufficient diagonal group (1.73 ± 0.4) as compared to the insufficient diagonal flow group (1.89 ± 0.5) ($P=0.030$). In multivariate logistic regression analyses, the insufficient diagonal flow group was not significantly associated with in-hospital death (HR 1.416, 95% CI 0.197–10.161, $P=0.729$) after controlling confounding

factors including hemodialysis, IABP support, EF, triple vessel disease, initial LAD flow, and initial diagonal flow (Table 4).

We also investigated in-hospital outcomes of STEMI patients whose culprit lesion was a diagonal branch ($n=11$) (isolated diagonal branch AMI). The in-hospital death was observed in two patients (18.2%), and mechanical complication was also observed in two patients (18.2%), which were higher than the sufficient diagonal flow group or the insufficient diagonal flow group.

Table 2 Lesion and procedural characteristics between the sufficient and insufficient diagonal flow groups

Variables	Sufficient diagonal flow (<i>n</i> = 170)	Insufficient diagonal flow (<i>n</i> = 59)	<i>P</i> value
Vessel number			0.003
1 vessel	127 (74.7)	30 (50.8)	
2 vessels	27 (15.9)	19 (32.2)	
3 vessels	16 (9.4)	10 (16.9)	
Initial TIMI (LAD)	1.3 ± 1.2	0.8 ± 1.0	0.006
Initial TIMI (diagonal)	2.0 ± 1.3	1.1 ± 1.2	< 0.001
Final TIMI (LAD)	3.0 ± 0.0	3.0 ± 0.0	–
Final TIMI (diagonal)	3.0 ± 0.0	1.0 ± 0.8	< 0.001
Mean stent diameter (mm)	2.78 ± 0.32	2.87 ± 0.33	0.07
Stent length (mm)	23.2 ± 7.8	24.0 ± 7.3	0.386
Stent			0.305
Bare metal stent, no. (%)	7 (4.1)	4 (6.8)	
BP-SES, no. (%)	8 (4.7)	0	
BP-EES, no. (%)	13 (7.6)	2 (3.4)	
EES, no. (%)	96 (56.5)	34 (57.6)	
ZES, no. (%)	44 (25.9)	17 (28.8)	
POBA alone	2 (1.2)	2 (3.4)	
Access site			
Radial artery, no. (%)	113 (66.5)	29 (49.2)	0.018
Brachial artery, no. (%)	5 (2.9)	5 (8.5)	0.440
Femoral artery, no. (%)	51 (30.0)	27 (45.8)	0.028
Catheter size			0.055
6 Fr, no. (%)	121 (71.2)	34 (57.6)	
7 Fr, no. (%)	49 (28.8)	25 (42.4)	
Aspiration, no. (%)	41 (24.1)	15 (25.4)	0.841
Performed IVUS pre stenting	167 (98.2)	58 (98.3)	0.972
Wire protect	42 (24.7)	12 (10.3)	0.496
Jail of diagonal	121 (71.2)	49 (83.1)	0.072
Rotablator useno (%)	3 (1.8)	3 (5.1)	0.169
LMT-LAD crossover stenting	14 (8.2)	5 (8.5)	0.954
Kissing balloon technique	7 (4.1)	1 (1.7)	0.383
2 stent technique	1 (0.6)	0	0.555

Data are expressed as the mean ± SD or number (percentage). A Student's *t* test was used for normally distributed continuous variables, a Mann–Whitney *U* test was used for abnormally distributed continuous variables, and a Chi-square test was used for categorical variables

BP-SES biodegradable-polymer sirolimus-eluting stent, *BP-EES* biodegradable-polymer everolimus-eluting stent, *EES* everolimus-eluting stent, *ZES* zotarolimus-eluting stent, *POBA* percutaneous old balloon angioplasty, *IVUS* intra-vascular ultrasound, *LMT* left main trunk, *LAD* left anterior descending artery

Table 3 Clinical outcomes between the sufficient and impaired diagonal flow groups

Variable	Sufficient diagonal flow (<i>n</i> = 170)	Impaired diagonal flow (<i>n</i> = 59)	<i>P</i> value
Mechanical complication, no. (%)	2 (1.2)	0	0.403
In-hospital death, no. (%)	5 (2.9)	5 (8.5)	0.073
Heart failure at discharge, no. (%)	56 (32.9)	25 (42.4)	0.192
Thrombus in left ventricular, no. (%)	4 (2.4)	4 (6.8)	0.117
Left ventricular wall motion score index	1.73 ± 0.4 (155/170)	1.89 ± 0.5 (53/59)	0.030

Data are expressed as the mean ± SD or number (percentage). A Student's *t* test was used for normally distributed continuous variables, a Mann–Whitney *U* test was used for abnormally distributed continuous variables, and a Chi-square test was used for categorical variables

Table 4 Multivariate logistic regression analysis predicting in-hospital death

Variables	HR	95% CI	P value
Impaired diagonal flow (vs. sufficient diagonal flow)	1.416	0.197–10.161	0.729
Hemodialysis	0.248	0.026–2.355	0.248
IABP	0.419	0.047–3.770	0.438
EF	0.889	0.829–0.954	0.001
TVD	1.160	0.149–9.017	0.887
Initial TIMI flow of LAD	1.359	0.517–3.573	0.534
Initial TIMI flow of diagonal	1.141	0.435–2.995	0.788

MACE major adverse cardiac event, *IABP* intra-aortic balloon pumping, *EF* ejection fraction, *TVD* triple vessel disease, *LAD* left anterior descending artery

Discussion

The present study included consecutive 229 LAD-STEMI patients whose final LAD flow was maintained (TIMI-3) by PCI, and those patients were divided into the sufficient diagonal flow group ($n = 170$) and the insufficient diagonal flow group ($n = 59$). The in-hospital outcomes were comparable between the two groups. Of note, the mechanical complications including cardiac rupture, ventricular septal perforation, and acute mitral regurgitation due to papillary muscle rupture were not observed in the insufficient diagonal flow group. Our results suggest that the insufficient diagonal flow in acute phase may not be associated with worse in-hospital outcomes, as long as the LAD flow is maintained in patients with anterior STEMI.

Although an early study reported that the incidence of mechanical complications is greater when the culprit of AMI is side branch [7], there were no mechanical complications in the present study when insufficient diagonal flow was observed in anterior STEMI. It is important to address the reason of the difference between the early study and the present study. First, since the global left ventricular systolic function is usually maintained after the side branch (diagonal branch) AMI [17], there would be a gap in left ventricular wall motion as well as wall thickness between the infarcted area caused by diagonal branch occlusion and the non-infarcted area. That gap could be a cause of mechanical complications [18]. On the other hand, the global left ventricular systolic function is decreased after the LAD-AMI with insufficient diagonal flow, there would be less gap in left ventricular wall motion as well as wall thickness between the infarcted area and the non-infarcted area in the LAD-AMI. In fact, the incidence of mechanical complications was greater in the diagonal branch AMI in the present study, indicating the higher risk of mechanical complications in the isolated diagonal branch AMI.

Although the frequency of in-hospital death tended to be higher in the insufficient diagonal flow group than in the sufficient diagonal flow group, that tendency disappeared after controlling confounding factors in multivariate logistic regression analysis. Our results may indicate that the severity of AMI was greater in the insufficient diagonal flow group than in the sufficient diagonal flow group. Thus, the difference of severity could affect the difference of in-hospital death in the present study. Therefore, our results do not support aggressive PCI to the diagonal branch as long as the LAD flow is maintained by PCI when the culprit of AMI is the LAD.

Clinical implications of our study should be discussed. If sufficient diagonal flow is not necessary in LAD-AMI, we can simplify the primary PCI to LAD. We may skip complex procedures such as kissing balloon technique or twostent strategy [19], and may concentrate on the openness of LAD (TIMI-3 flow in LAD). Since those complex procedures are associated with stent thrombosis or adverse events in primary PCI [5], simplified procedures would be safer than complex procedures in primary PCI. However, we should mention that the LVWMSI was better in the sufficient diagonal flow group as compared to the insufficient diagonal flow group. It may be better to take care of the flow of diagonal branch as long as the procedure is simple. On the other hand, the in-hospital outcomes of isolated diagonal branch-AMI were worse in the present study. If the culprit of STEMI is not a LAD, but a diagonal branch, it would be better to perform PCI to the diagonal branch. It is important to distinguish the isolated diagonal branch-AMI from LAD-AMI involving diagonal branch.

Study limitations

Since this study was a single-center retrospective observational study, there is a risk of patient selection bias and group selection bias. As the study population was not large enough, there is a possibility of beta error [20]. Although our multivariate logistic regression analysis did not show the significant association between in-hospital death and the insufficient diagonal flow group, the incidence of in-hospital death tended to be higher in the insufficient diagonal flow group, which may indicate the worse clinical outcomes in the insufficient diagonal flow group. Because our study did not address the long-term clinical outcomes, the advantage of PCI to diagonal branch in anterior STEMI might be underestimated in the present study design. Since the incidence of mechanical complication was low, we could not perform multivariable analysis using mechanical complication as dependent variable. Moreover, while cardiac rupture, ventricular septal perforation, or acute mitral regurgitation due to papillary muscle rupture were defined as mechanical complications in the present study, mechanical complication

related to the region of diagonal branch may be limited to free wall rupture and acute mitral regurgitation. The reason for low incidence of mechanical complications may be derived from the study design that the final LAD flow was TIMI-3 in all study population. Our results require further validation in the setting of prospective studies.

Conclusions

In-hospital outcomes were not significantly different between the sufficient and insufficient diagonal flow groups. We may not stick to the diagonal flow in LAD-STEMI, as long as the LAD flow is maintained by PCI.

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Compliance with ethical standards

Conflict of interest Dr. Sakakura has received speaking honoraria from Abbott Vascular, Boston Scientific, Medtronic Cardiovascular, Terumo, OrbusNeich, and NIPRO; has served as a proctor for Rotablator for Boston Scientific; and has served as a consultant for Abbott Vascular and Boston Scientific. Prof. Fujita served as a consultant for Mehergen Group Holdings, Inc. Other authors declare no conflict of interest.

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